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Economic Impacts of Mastitis in Canadian Dairy Herds

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Résumé

La mammite bovine cause des pertes économiques importantes et récurrentes sur l'industrie laitière dans le monde. L'objectif principal de cette étude était d'estimer les coûts associés à la mammite sur les fermes laitières canadiennes en 2015. Les cadres économiques de la mammite précédemment publiés ont été utilisés pour préparer un modèle économique avec les composantes de coûts les plus importantes. Un questionnaire a été conçu et envoyé par la poste à 374 producteurs laitiers choisis au hasard dans l'Étude Laitière Nationale du Canada 2015 pour recueillir des données sur ces composantes des coûts, et 145 (39%) producteurs laitiers ont retourné un questionnaire rempli. Pour chaque troupeau, les coûts liés aux différentes composantes liés à la mammite et la proportion des coûts attribuables à une composante spécifique ont été calculés. Les coûts de la mammite étaient importants (662 CAD par vache-an pour une ferme laitière canadienne typique), une grande partie des coûts (48%) étant attribuée à la mammite sub-clinique (SCM) et 34% et 15% à la mammite clinique (CM) et aux mesures préventives, respectivement. Pour la SCM, les deux composantes de coûts les plus importantes étaient la diminution de production laitière et la réforme subséquente (respectivement 72% et 25% des coûts de mammite sub-clinique). Pour la CM, la première, la deuxième et la troisième composante des coûts étaient, respectivement, la réforme (48% des coûts de CM), la réduction du rendement laitier dû à la CM (34%) et, finalement, le lait jeté suite à la mammite (11%). Cette étude est la première depuis 1990 à étudier les coûts de la mammite au Canada. Les chiffres obtenus dans la présente étude pourraient être utilisés pour créer un modèle économique pour calculer les coûts de la mammite au niveau troupeau et au niveau national au Canada.

Mots-clés : vache laitière, mammite, économique, Canada

Abstract

Mastitis imposes significant and recurring economic losses on the dairy industry worldwide. The main objective of this study was to estimate costs associated with mastitis on Canadian dairy farms in 2015. Previously published mastitis economic frameworks were used to develop an economic model with the most important cost components. A questionnaire was designed and mailed to 374 dairy producers randomly selected from the Canadian National Dairy Study 2015 to collect data on these costs components, and 145 (39%) dairy producers returned a completed questionnaire. For each herd, costs due to the different mastitis-related components and the proportion of the costs attributable to a specific component were computed. Mastitis costs were substantial (662 CAD/milking cow-year for a typical Canadian dairy farm), with a large portion of the costs (48%) being attributed to sub-clinical mastitis (SCM), and 34% and 15% due to clinical mastitis (CM), and implementation of preventive measures, respectively. For SCM, the two most important cost components were the subsequent milk yield reduction and culling (72% and 25% of SCM costs, respectively). For CM, first, second, and third most important cost components were culling (48% of CM costs), milk yield reduction following the CM events (34%), and discarded milk following mastitis (11%), respectively. This study is the first since 1990 to investigate costs of mastitis in Canada. The figures obtained in the current study could be used to develop an economic model to compute mastitis costs at the herd and the national level in Canada.

Keywords: dairy cow, mastitis, economic, Canada

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List of Abbreviations

BMSCC:	Bulk tank milk somatic cell count
cfu:	Colony forming unit
CM:	Clinical mastitis
CNS:	Coagulase negative staphylococci
DHI:	Dairy herd improvement
IMI:	Intramammary infection
IRCM:	Incidence Rate of Clinical Mastitis
mL:	Millilitre
PCR:	Polymerase chain reaction
SCM:	Subclinical mastitis
SCC:	Somatic cell count
SCS:	Somatic cell Score

Dedicated to Iranian Female veterinarians and my beloved family

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Introduction

Mastitis continues to be one of the costliest diseases in dairy farming despite all advances in control and preventive measures. Mastitis lowers the quality and quantity of produced milk by inducing pathologic changes in mammary glands. Causing direct damage to milk production distinguishes mastitis from other economically significant diseases of dairy cows such as reproduction diseases and lameness (Halasa et al., 2007b, Ruegg, 2012). Regarding increased concerns of dairy product consumers about animal welfare and food safety, mastitis remains a challenging issue for the profitability and sustainability of dairy industry (Noordhuizen and Metz, 2005). Controlling this endemic disease is very challenging not only because it is multifactorial, but also because it can be caused by numerous pathogens which are capable of surviving in cow mammary gland or environment for a long time (Huijps et al., 2010).

Knowing the costs of mastitis is essential for dairy producers and their advisors to make decisions regarding the control and treatment strategies. A part of mastitis costs can be estimated using models developed by previous studies. For example, some models have been used to estimate the amount and value of milk yield reduction subsequent to clinical mastitis (CM) or subclinical mastitis (SCM) (Gröhn et al., 2005, Halasa et al., 2009, Hertl et al., 2014b). These models could certainly be used in different countries and settings. However, other components of mastitis costs (e.g. costs of drugs, labor, materials and investments) may vary among countries and are influenced by some factors such as resource prices, cost of milk production, policies controlling the dairy market, and producers' preferences for adopting prevention measures. For these reasons, studies on mastitis costs estimation should be conducted based on source populations restricted to one geographical region such as a country or even a state (Weigler et al., 1990, Seegers et al., 2003a, Pérez-Cabal et al., 2008).

In studies that estimate the costs of mastitis, total cost was generally divided into different categories. In Halasa et al. framework (2007c), cost of mastitis is divided into ten cost components including: 1) milk production loss, 2) drugs, 3) discarded milk, 4) veterinary services, 5) labor, 6) milk quality, 7) diagnosis, 8) culling, 9) other diseases, 10) material and investments. In another classification, total mastitis costs consisted of economic loss and expenditures (McInerney et al., 1992a, Bennett et al., 1999). The term “economic loss” implies decrease in output or benefit, like milk yield reduction or culling. The term “expenditure” implies any additional inputs or resources that were not planned, for example, CM treatment. The term “economic cost” is a general term used to refer to any form of economic consequence including expenditures or economic losses (McInerney et al., 1992b, Bennett et al., 1999). In another classification system, costs were broken down into two categories. First, failure costs which are direct costs associated with treatment, culling, or production loss due to mastitis. Second, preventive costs which includes the money and time spent on practices performed for mastitis prophylaxis (van Soest et al., 2016b).

A part of mastitis costs is called direct costs as it is easier for dairy producers to identify these, for instance, treatment costs (e.g., expenditures for drugs and extra labor), costs of veterinary services, costs of discarded milk. Nevertheless, the other part of mastitis costs (i.e. indirect or hidden costs) is more difficult to perceive (Østeras, 2000). Reduced milk production and involuntary culling are examples of indirect costs that producers may not notice or not know the values of these costs. This could be one of the reasons explaining that dairy producers usually underestimate costs of mastitis (Petrovski, 2006, Huijps et al., 2008b).

The only study found by authors conducting an economic analysis of mastitis in Canadian dairy farms (Gill et al., 1990a) did not estimate the total cost of mastitis. In this latter study, adoption rate and efficiency of some management practices for mastitis treatment and prevention were investigated. Since then, no recent studies were conducted to evaluate the economic impacts of mastitis on Canadian dairy farms. Therefore, there is no recent study reporting on total cost of mastitis on Canadian dairies. The objective of this thesis was to appraise these costs, in the most comprehensive manner, and using current figures from a large sample of Canadian dairies.

Chapter 1 - Literature Review

Mastitis remains a challenging disease in dairy farming all over the world despite all the researches and efforts implemented to control it. This may be due to the fact that it is a complex disease with numerous determinants including those related to cows, their environment, and the microorganisms (Table I). Mastitis results in considerable economic losses. It is recognised as the most costly disease of dairy cows (Schepers and Dijkhuizen, 1991, Ruegg, 2003, Seegers et al., 2003b).

Table I. Determinants of mastitis; adapted from Thrusfield (2007)

Host:	Age
	Breed
	Stage of dry period
	Stage of lactation
	Teat and udder condition
	Host resistance
	others
Agent	(over 140 microorganisms)
	Virulence
	Resistance to antimicrobials
	Host adaptation
	others
Environment	Bedding
	Stall
	Temperature
	Humidity
	Density (herd size)
	Management practices used
	others

1. Mastitis

Mastitis is defined as an inflammation of the mammary gland which occurs mainly due to infection by bacteria. After the microorganisms enter the teat canal and multiply in the milk, they will encounter several defense mechanisms of the organ. If the defence mechanisms are impaired such as during periparturium period or if the microorganisms can evade all these barriers, intramammary infection (IMI) is then established. The severity of the inflammatory response elicited by the microorganism determines the mastitis status: clinical vs. subclinical mastitis (Zhao and Lacasse, 2008).

1.1 Clinical Mastitis

Clinical mastitis (CM) is a condition in which the IMI induces clinical features such as visible changes in milk with or without local (i.e. the mammary gland quarter) or systemic signs. The milk may contain clot, blood, fibrin, pus, or show alterations in color or consistency. A scoring system was proposed to score CM (Sears and McCarthy, 2003). When clinical signs include only visible changes in milk, CM severity is scored 1 (i.e. mild CM). When the signs (erythema, pain, heat, and swelling) are restricted to the mammary gland a severity score of 2 (i.e. moderate severity) is assigned. With more severe inflammatory response, systemic clinical features such as anorexia, fever, shock, and even death occurs. Such cases are defined as severe CM and scored 3 on the severity scale (Philpot and Nickerson, 2000, Sears and McCarthy, 2003b).

Incidence Rate of Clinical Mastitis (IRCM) in Canada

Based on data from a cohort of 106 dairy farms, the overall mean and median IRCM in Canada were respectively 23.0 and 16.7 cases/100 cows-years between 2003 and 2005 (Figure 1) (Olde Riekerink et al., 2008). The mean IRCM in the different Canadian provinces are reported in Table II. Important differences in IRCM could be seen between provinces. Such differences may be caused by factors such as geographic region, housing system, and mean bulk tank milk somatic cell count (**BMSCC**) which varied widely among provinces.

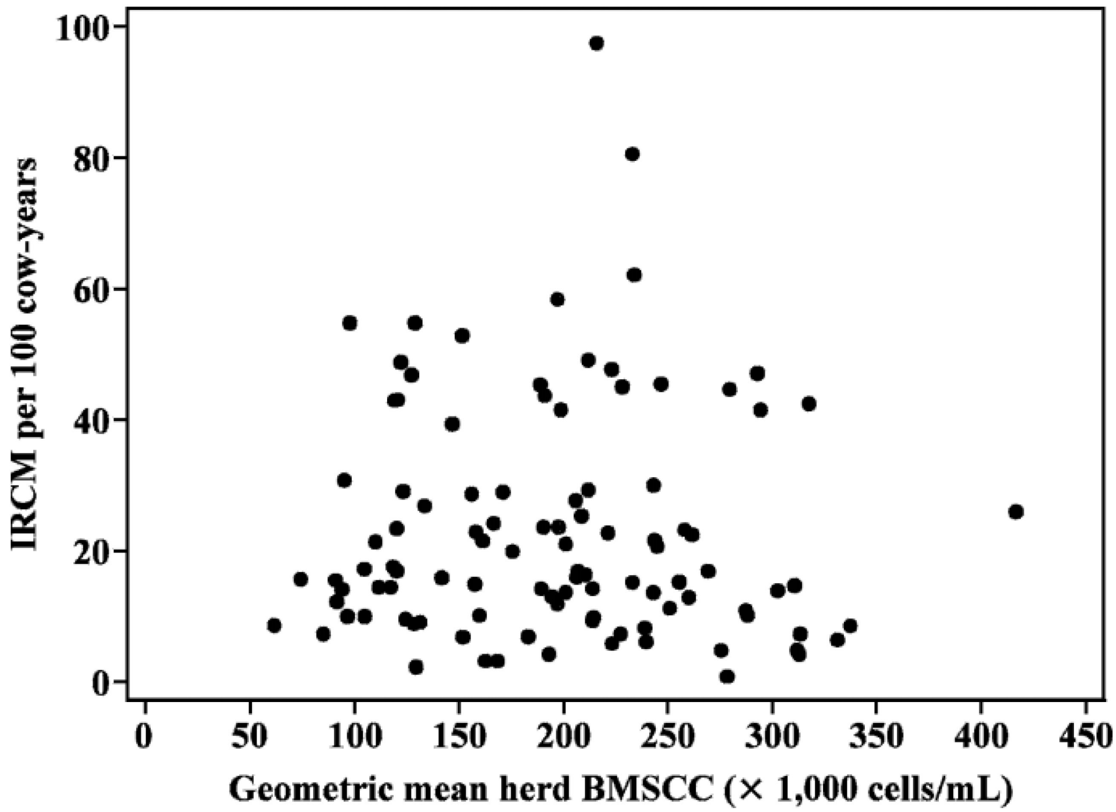

Figure 1. IRCM variation in different herds with different BMSCC; reproduced from Olde Riekerink (2008)

Incidence rate of CM varies among herds regardless of herd BMSCC, and no linear relation between IRCM and BMSCC has been demonstrated (Figure 1). That is why mastitis control programs should be tailored to the needs of the farm, and one single program is not applicable to all dairy systems (Olde Riekerink et al., 2008). Clinical mastitis can be caused by environmental or contagious pathogens. The most frequently isolated bacteria from milk samples collected on day of CM diagnosis in the study by Olde Rikierink et al. (2008) were *Staphylococcus aureus* (10.3%), *Escherichia coli* (8.4%), *Streptococcus uberis* (6.3%), and coagulase-negative staphylococci (5.1%), but the most frequent finding was negative culture samples (43.9%). In Quebec *S. aureus* and *S. dysgalactiae* IRCM were highest.

Table II. IRCM in different provinces in Canada; adapted from Olde Riekerink (2008)

Province	Number of herds	Number of CM cases	Total cow-years at risk	Mean IRCM/100 cow-year	95% CI
British Columbia	8	216	1,427	14.2	8.5-23.6
Alberta	10	225	1,210	20.2	12.8-31.9
Saskatchewan	5	73	535	14.2	7.3-27.4
Manitoba	8	60	1,395	7.6	4.3-13.3
Ontario	16	433	1,633	31.6	22.0-45.4
Quebec	26	565	1,899	29.7	22.4-39.5
New Brunswick	6	82	423	22.8	12.0-43.2
Nova Scotia	10	155	1,300	14.0	8.7-22.4
Prince Edward Island	16	230	1,278	18.6	12.8-27.0
Newfoundland	1	113	378	29.9	7.4-120.2
Total	106	2,152	11,477	23.0	

Another cohort study performed in Canada during 2007 and 2008 on 91 herds is described in Reyher et al. (2011). In this latter study, the most common pathogens isolated from milk samples collected at diagnostic of CM were *S. aureus* (13%), *E. coli* (11%), and *Enterococcus* spp (8%). Culture negative samples constituted 27% of samples of clinical cases (Reyher et al., 2011). Using data from 69 herds from this later study, Eghafghuf et al. (2014) computed a mean IRCM of 21.3 CM cases/100 cow-year with 25th and 75th percentiles of 12.3 and 27.9 CM cases/100 cows-year. In the Elghafghuf's study, however, only the first case of

CM for a given cow and in a given lactation was considered. Furthermore, only herds demonstrating a minimum level of compliance in recording CM cases were considered. This later detail is of importance since it is well known that CM cases are often grossly underreported by dairy producers (Vaarst et al., 2002). In comparison, in the Olde Riekerink's study, second and third cases were also included in IRCM calculation, and herds included were not chosen based on CM recording completeness. Therefore, these IRCM can hardly be compared. In various study conducted around the world (Netherlands, France, USA, and Finland) mean IRCM ranging between 20 and 40 CM cases/100 cows-year have been reported, illustrating the relatively high incidence of this disease worldwide (Weigler et al., 1990, Bartlett et al., 1992, Barkema et al., 1998, Kossaibati et al., 1998, Barnouin et al., 2005, Heikkila et al., 2012).

Occurrence of CM as a function of lactation stage

Incidence rate of CM is highest in the first week after parturition (Barkema et al., 1998), then dramatically declines in the second week of lactation, and continues to decrease until the end of lactation (Olde Riekerink et al., 2008). This pattern is evident in Figure 2 and 3. It was demonstrated that, in more than 50% of the enterobacterial CM cases occurring in early lactation, the infections originated from the dry period (Bradley and J., 2000).

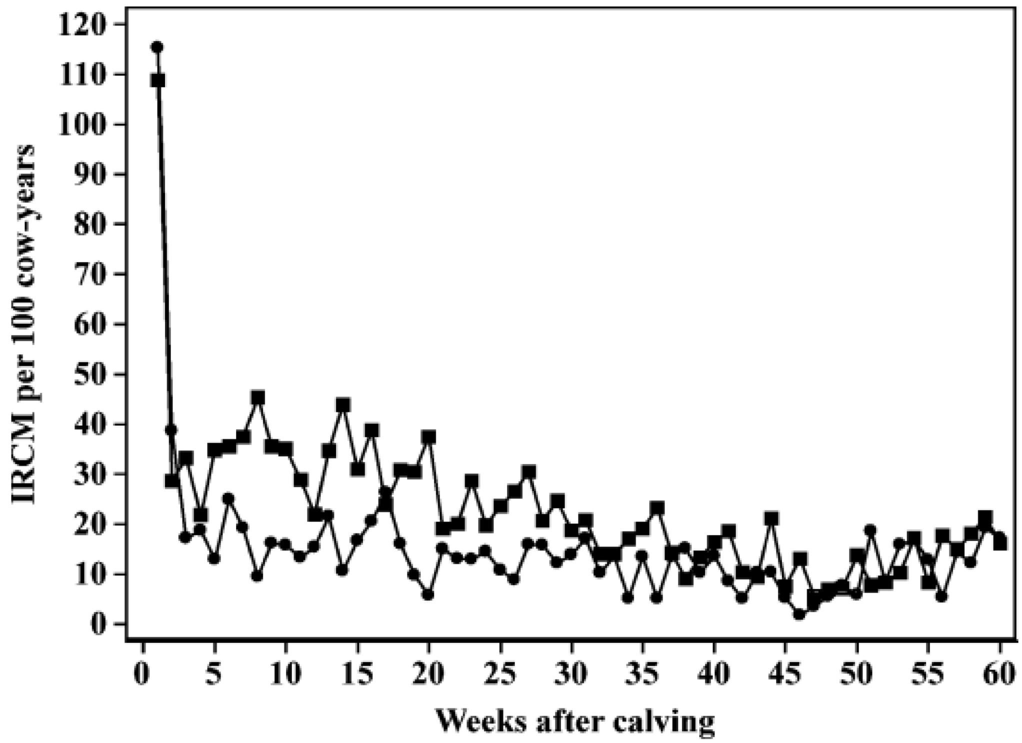

Figure 2. IRCM in weeks after calving in heifers (●) and adult cows (■); reproduced from Olde Riekerink (2008)

As it is shown in Figures 2 and 3, increasing parity is also associated with higher IRCM (Bradley, 2002, Elghafghuf et al., 2014). It is hypothesized that cow aging, compromises the efficiency of the defense mechanisms in mammary glands or the whole immune system (Weng, 2006). In addition, longer life time in older cows results in more exposure to microorganisms, and higher risk of IMI comparing to younger cows, consequently clinical flare-ups occurs more frequently in older cows (Elghafghuf et al., 2014). Teat end hyperkeratosis (callosity) is also more common in older cows because of the longer exposure to milking machine (Neijenhuis et al., 2001) and has been associated with higher odds of IMI acquisition (Dufour et al., 2012b).

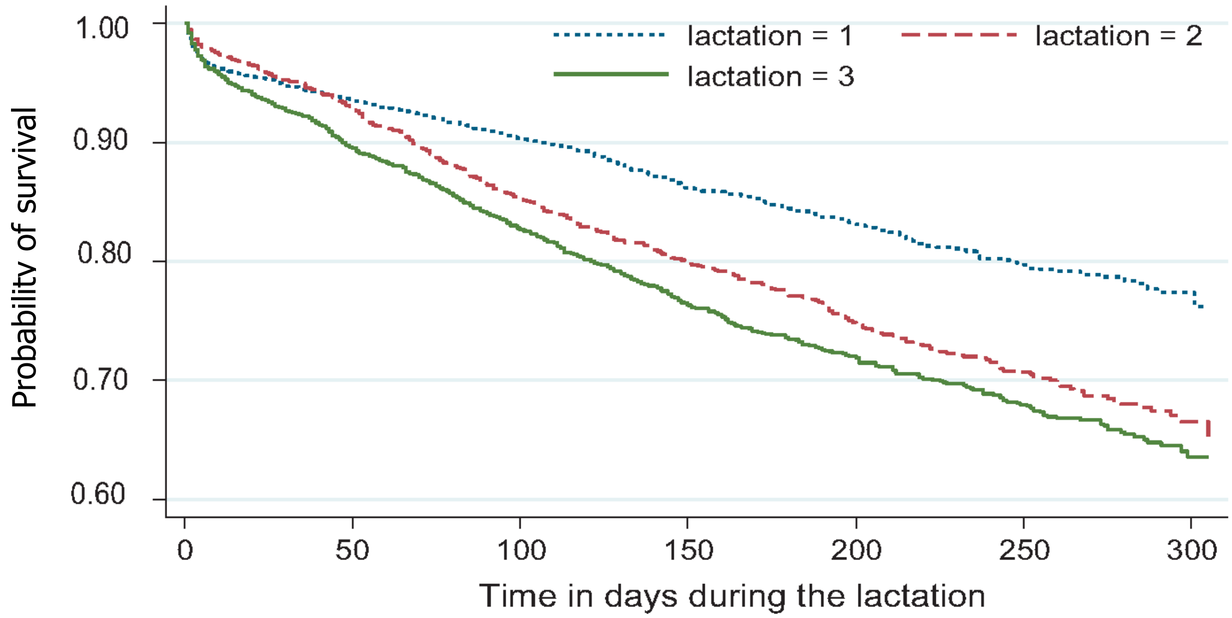

Figure 3. Kaplan-Meier survival curves for CM in 1st, 2nd, and 3rd lactation ; reproduced from Elghafghuf (2014)

1.2 Subclinical mastitis

The term subclinical mastitis (**SCM**) can be used to describe an inflammation of the mammary gland that is neither accompanied by visible abnormality of milk or the udder, nor by systemic signs. Alike CM, SCM is generally the result of an IMI caused by bacteria. Although signs of inflammation are not visible, milk yield is often reduced and milk composition is changed. Laboratory tests (e.g. somatic cell count, milk bacteriological analyses) are required to diagnose this condition. In the study by Djabri et al. (2002) mean SCC of healthy and infected quarter milk samples were compared. It was demonstrated in this latter study that intramammary infections caused by different pathogens result in different elevations in SCC (Tableau III). Subclinical mastitis is often of longer duration than CM and, therefore, more prevalent. Subclinical mastitis also causes greater economic losses compared to CM, mainly due to the sustained decreased milk production (Halasa et al., 2007a). After treatment of SCM, the production level does not usually get back to pre-mastitis level (St.Rose et al., 2003).

Table III. Geometric mean SCC in IMI induced by different pathogens; adapted from Djabri et al. (2002)

IMI agent	Geometric mean SCC (x1,000 cells/ml)
Coliforms	4,196
S. agalactiae	1,129
S. Uberis	1,024
S. dysgalactiae	547
S. aureus	333
Corynebacterium bovis	167
Staphylococci other than *S. aureus*	155
Healthy quarters	68

Unlike IRCM which showed no linear relation with BMSCC (Olde Riekerink et al., 2008), SCM is closely related to individual and herd somatic cell counts (SCC), and is often diagnosed using these measurements. Milk cytologic assessment and bacteriological culture are routine laboratory methods used to diagnose SCM. The exact SCC threshold that could be used to differentiate SCM from healthy mammary gland is still a subject of debate. However, one of the most frequently suggested cut-off points is 200,000 cells/ml (Dohoo and Leslie, 1991, Schukken et al., 2003, Piepers et al., 2007). Coagulase negative staphylococci (CNS) are the agents most frequently isolated from apparently normal milking quarters in many countries (Dohoo and Leslie, 1991, Tenhagen et al., 2006, Piepers et al., 2007, Pyorala and Taponen, 2009). Some other species that were identified to cause SCM include *S. aureus*, *Corynebacterium bovis*, *S. agalactiae*, *S. dysgalactiae,* and *S. Uberis* (Zadoks et al., 2003).

Incidence rate of SCM in Canada

In a study by Dufour et Dohoo (2013) conducted on 91 Canadian dairies, the median herd incidence rate of SCM was estimated, using milk bacteriological culture results, at 0.17 new IMI per quarter-month, with 25th and 75th percentiles of 0.08 and 0.36 new IMI/quarter-month. This would mean that, in a typical Canadian herd, 17% of healthy quarters would become infected each month (compared to 1.8% of cows experiencing a CM each month; i.e. 21.3 CM cases/100 cow-year divided by 12 months). Incidence estimates (i.e. number of new cases per animal-time unit) are, however, relatively uncommon for SCM since their estimation require multiple repeated sampling of quarters. More often, prevalence (i.e. proportion of animal infected at a given point in time) are reported. In these same 91 Canadian dairies, a SCM prevalence of 44% was observed (Reyher et al., 2011). In a study performed in the Netherlands, cows were categorized in two groups of high SCC (>250 000 cells/ml) and low SCC (<150 000). Subclinical mastitis prevalence of respectively 79.2% and 54.3% were observed in each group (Sampimon et al., 2009). Studies in Germany and Belgium using bacteriological culture showed prevalence of SCM of 26.4% (Tenhagen et al., 2006) and 41.4% respectively (Piepers et al., 2007).

Subclinical mastitis occurrence in different stages of lactation

Nearly 50% of environmental IMIs are initiated during the dry period (Todhunter et al., 1995a). In term of IMI risk, the dry period can be separated in three stages. The risk of new IMI is higher in the first and last stages of the dry period (Bradley and Green, 2004) as illustrated in Figure 4. The first stage is named “involution” and usually last for 10 to14 days until the protective keratin plug is completely formed. Moreover, the teat canal is dilated in this stage as a result of physiologic atrophy in teat canal epithelium (Comalli et al., 1984). Cessation of milking which removes bacteria through flushing is another factor that increases the risk of new IMI in the involution stage. Immunoglobulin and lactoferrin concentrations are also low and leukocyte functions are impaired during involution. The second stage called “involuted state” is the time when mammary glands are highly protected by means of defence mechanisms, and this stage last until three weeks prior to calving. The insufficient keratin plug and teat dilation then recur during the last stage, named the “colostrogenesis”. The Immunoglobulins and lactoferrin are again diluted in this last phase, which consequently increases mammary gland susceptibility to pathogens (Cousins et al., 1980, Sordillo and Nickerson, 1988). After parturition, IMI incidence declines until the end of lactation (Bradley and Green, 2004).

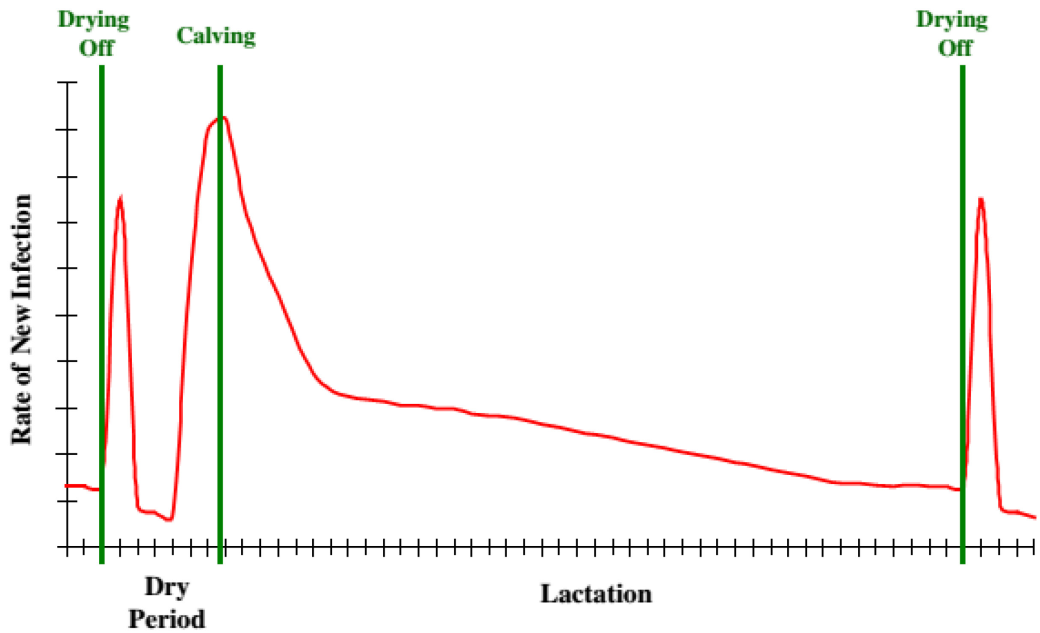

Figure 4. Schematic diagram of IMI incidence in different stages of the dry period and lactation; reproduced from Bradley and Green (2004)

1.3 Categorization as environmental vs. contagious intramammary infection

The agents that may cause mastitis are often classified as environmental or contagious pathogens, depending on most probable origin of the causative agent (Bramley and Dodd, 1984, Sandholm et al., 1990). Environmental microorganisms mainly reside in the environment of cows and the probability of cow to cow transmission is minimal. These agents include coliforms and some streptococcal species and are most often associated with CM. Pre-milking teat disinfection and increasing the hygiene of the cow environment are important strategies to control these agents (Bartlett et al., 1992b, Smith and Hogan, 1993).

Conversely, contagious agents are mainly transmitted from infected quarters during milking by means of milkers' hands and milking unit. Contagious pathogens most often cause SCM (Fox and Gay, 1993). Efficient techniques to control contagious agents are post-milking teat disinfection, dry cow therapy, proper maintenance of milking system, and culling of chronically infected cows. Prominent contagious agents are *S. aureus*, *S. agalactiae*, and *Corynebacterium bovis* (Fox and Gay, 1993, Blowey and Edmondson, 2010).

1.4 Most common pathogens

Gram positive bacteria

Staphylococci are recognized as the most commonly isolated bacteria in SCM cases (Pitkälä et al., 2004). According to their ability to coagulate rabbit plasma, these bacteria are divided into two categories; coagulase positive staphylococci (**CPS**) including most strains of *S. aureus* and *S. hyicus* and coagulase negative staphylococci (**CNS**) (Taponen and Pyörälä, 2009).

Staphylococcus aureus. *S. aureus* often causes a persistent SCM with important increase in SCC. The mean duration of *S. aureus* IMI until spontaneous elimination occurs is estimated at 25.5 weeks (Grommers and Van De Geer, 1985). As shown in Table III, geometric mean SCC of quarters harboring *S. aureus* IMI was estimated at 333,000 c/mL (Djabri et al., 2002). However, it can also result in CM with moderate to severe local and systemic signs (Myllys, 1995). In certain conditions, infection by *S. aureus* may result in acute gangrenous mastitis (Le Maréchal et al., 2011). *Staphylococcus aureus* is one of the two microorganisms with the highest IRCM (3.98 cases/100 cows-year) in Quebec (Olde Riekerink et al., 2008). In another study, *S. aureus* was known as the most frequently isolated contagious agent in Quebec (Francoz et al., 2012). Little improvement has been achieved in herd-level prevalence of *S. aureus* over the last 20 years in Quebec (Francoz et al., 2012). A mean incidence rate of *S. aureus* IMI of 0.012 new IMI per quarter-month was estimated in Canada and the mean quarter prevalence was estimated to be 3.9% (Dufour et al., 2012b).

There is a positive correlation between teat lesions and *S. aureus* colonization (Fox and Cumming, 1996). Increased callosity of teat is also associated with higher odds of *S. aureus* IMI (Dufour et al., 2012b), whereas wearing gloves by milkers and pre- and post-milking teat disinfection are recognized as important risk factors associated with lower *S. aureus* IMI incidence and prevalence (Dufour et al., 2012b).

An important stage in the pathogenesis of *S. aureus* is attachment to the host cells (Dego et al., 2002). Other virulence factors of these bacteria include biofilm formation and invasion into mammary epithelial cells that makes the bacteria inaccessible to immune responses and antibiotics. Production of haemolysin, leucocidin, exfoliative toxins, enterotoxins, and toxic-shock syndrome toxin are also known virulence factors of *S. aureus* (Cucarella et al., 2004).

Mastitis caused by *S. aureus* does not respond well to antibiotic treatments. The chance of bacteriological cure in such cases varies from 15% to 85% depending on physiologic status of the cow and virulence of infecting strain (Barkema et al., 2006). Longer periods of intramammary treatment i.e. 5 to 8 days using pirlimycin (Deluyker et al., 2005) or ceftiofur (Oliver et al., 2004) have shown a positive association with cure rates (Roy and Keefe, 2012). The poor response to treatment may stem from the fibrous tissue that surrounds the bacteria in the mammary gland and impedes the penetration of antibiotics. Furthermore, *S. aureus* can survive in macrophages, neutrophils and epithelial cells (Blowey and Edmondson, 2010).

Coagulase negative staphylococci (CNS). Coagulase negative staphylococci are normal flora of the cow skin with the potential to initiate mastitis as opportunistic microorganisms (Devriese and De Keyser, 1980). Twenty-four species of CNS are isolated from dairy cattle milk samples so far (Vanderhaeghen et al., 2014), but a few are more common. The main species isolated from bedding and housing includes *S. xylosus, S. sciuri, S. saprophyticus* (Matos et al., 1991). These species are also isolated from cow skin, hairs, nostrils, and teat. Other species like *S. chromogenes, S. warneri, S. epidermidis* are also isolated from cow skin in other surveys (Devriese and De Keyser, 1980). Among CNS, the most commonly isolated species from IMI are *S. chromogenes, S. epidermidis, S. haemolyticus, S. simulans, S. xylosus* (Fry et al., 2014, Vanderhaeghen et al., 2014). Coagulase negative staphylococci used to be regarded as minor microorganisms that usually infect heifers in the periparturition period. They rarely induce clinical signs (Schukken et al., 2009). These bacteria cause a slight increase in SCC as described in Table Ⅲ, and are often eliminated from the mammary gland in a short time after parturition (Myllys, 1995). However, nine species were isolated from persistent IMI in a study by Fry et al. (2014) using isolates from the Canadian Bovine Mastitis and Milk Quality Research Network (CBMQRN) culture collection. The median interval between first and last CNS positive samples was estimated at 21 days in this study, but this duration may not precisely represent CNS IMI duration because the onset of infection was unknown in some cases.

In a cohort study by Dufour et al (2012a) on 90 Canadian dairy farms in 2007 and 2008, the mean quarter prevalence of CNS IMI was estimated as 42.7%. Incidence and elimination rate were also reported to be 0.29 and 0.79 IMI/quarter-month, respectively. In that study by Dufour and colleagues, milk samples with ≥100 cfu/ml were considered as positive for CNS IMI. In Belgium, a quarter prevalence of 42% in heifers during early lactation was observed using a threshold of ≥200 cfu/ml to define CNS IMI (Piepers et al., 2011). In Germany and the Netherlands, the prevalence was respectively 8-11% and 10-15%. Each study considered milk samples ≥1000 and ≥500 cfu/ml as a definition for CNS IMI (Tenhagen et al., 2006b, Sampimon et al., 2009). Since different thresholds were used to define IMI, the results of these studies cannot directly be compared.

In a recent study in Canada, CNS bacteria isolated from milk samples where identified using mass spectrometry, and *S. chromogenes, S. epidermidis,* and *S. haemolyticus* were reported to constitute 29%, 13%, and 10% of isolated CNS bacteria (Cameron et al., 2017). Whereas, in another study by Fry et al. (2014) *Staphylococcus chromogenes* (48% of isolates)*, S. simulans* (19%)*,* and *S. xylosus* (10%) were identified as three most prevalent CNS species. The first two species could cause persistent IMI (median IMI duration of 21 and 28 days, for *S. chromogenes* and *S.* simulans, respectively) with remarkable increase in SCC (median SCC of 171,000 and 265,600 cells/mL) (Fry et al., 2014). The incidence rate of CNS IMI using tDNA-PCR was reported at 5.8% quarters/month in Belgium (Supré et al., 2009). In a study by Trinidad (1990) the quarter prevalence of *S. chromogenes* IMI was 43.1%.

Streptococcus agalactiae. These bacteria are gram positive cocci, known to be greatly contagious and obligatory parasite of the cow mammary glands (McDonald, 1977). During infection, they mainly reside in the lower ducts. However, these bacteria have the potential to spread to the whole glandular tissue of the infected quarter. *Streptococcus agalactiae* adheres well to the epithelial cells in mammary gland which is an important stage in their pathogenesis (Frost et al., 1977). As a consequence to the host inflammatory response, leukocytes infiltrate in this area. The bacterial and cell debris occludes the ducts which results in a substantial reduction in milk production in the current and subsequent lactation period. The IMI due to *S. agalactiae* rarely causes systemic illness. These are usually persistent IMI with possible intermittent flare-ups of CM. (Jain, 1979). In a meta-analysis by Djabri (2002) the geometric mean SCC of *S. agalactiae* infected quarters was 1,129,000 cells/mL which is estimated to be a 12.6-fold increase of SCC compared to healthy quarters.

S. agalactiae was the major cause of chronic mastitis in pre-antibiotic era, but since it is sensitive to many antibiotics and it does not survive in the environment, it is possible to eradicate this disease (Jain, 1979). Estimated province-stratified herd-level prevalence of *S. agalactiae* in Canada was 4.4% in 2010. The herd-level prevalence of this agent is considerably reduced in last decades which supports the idea that IMI due to *S. agalactiae* is on its way to be eradicated in Canada (Olde Riekerink et al., 2010).

Streptococcus dysgalactiae. This agent is not an obligate udder pathogen and survives in the environment for a long time. Thus, it is difficult to eradicate. Mastitis due to *S. dysgalactiae* is usually subclinical (Todhunter et al., 1995b). *Streptococcus dysgalactiae* is frequently isolated from infected quarters and injured teats and can be transmitted during milking (Bramley and Dodd, 1984). This is a characteristic of contagious organisms. However, *S. dysgalactiae* may also reside in extramammary sites like cow nostril, vagina, and tonsils and infect non-lactating cows which are characteristics of environmental agents (Bramley and Dodd, 1984, Colque et al., 1993). It is commonly isolated from teat skin especially when there are skin lesions on the teat. Therefore, isolation of *S. dysgalactiae* is recognised as one of the indicators for teat damage (Calvinho et al., 1998). This organism is also isolated from common cow fly *Hydrotaea irritans*. This fact confirms this fly role in transmission of *S. dysgalactiae* as of one the agents of summer mastitis (Bramley et al., 1985). In Quebec, *Strep dysgalactiae* is one of the two microorganisms with highest IRCM (Olde Riekerink et al., 2008). It is estimated that IMI due to *S. dysgalactiae* results in 5.7 times increase in SCC, and the geometric mean SCC of quarter infected by this pathogen was 547,000 c/mL(Djabri et al., 2002).

Streptococcus uberis. *Streptococcus uberis* is also frequently isolated from milk. This bacterial species is not an obligate udder pathogen, and can survive in the environment for long period. In chronic cases of *S. uberis* IMI, contagious transmission was also observed (Zadoks et al., 2001). The bedding material contaminated by cow feces and urine is mainly the source of *S. uberis* to which teats are exposed. Moreover, pastures and walking areas with high traffic of cows are other known reservoirs. (Gabler et al., 2001, Zadoks et al., 2005).

Other gram positive cooci. In addition to streptococci, some gram positive catalase-negative cocci such as *Enterococcus, Aerococcus* and *lactococcus spp* can cause mastitis (Wyder et al., 2011). These bacteria can be recovered from both clinical and SCM. Environmental streptococci can induce a considerable rise in SCC. Being able to survive in neutrophils, they have the potential to cause chronic IMI (Djabri et al., 2002). Although most Environmental streptococci IMI ends in spontaneous recovery, nearly one third of infected quarters may remain infected for more than one lactation (Todhunter et al., 1995a).

Corynebacterium bovis. This spherical to oval shaped bacterium is a minor contagious agent which is the second most prevalent (6%) bacteria isolated from milk samples of apparently normal milking cows in the Canadian National Cohort of Dairy Farms during 2007 and 2008 (Reyher et al., 2013). It is frequently identified as a contaminant in PCR tests on milk samples (Koskinen et al., 2010). This agent is capable of colonizing the streak canal. This characteristic contributes to its contagious nature. Having a very limited pathogenicity, *C. bovis* IMI are rarely accompanied by clinical features. They are often restricted to a slight elevation in SCC (Fox and Gay, 1993).

Trueperella pyogenes. This opportunistic bacteria that was formerly known as *Arcanobacterium pyogenes* is part of normal flora of upper respiratory tract and urogenital mucous membranes of cows. Infection by *T. pyogenes* often occurs following injury to mucous membranes by trauma or infection by other microorganisms. *T. pyogenes* is one of the major bacteria causing summer mastitis. In addition to mastitis, *T. pyogenes* may cause abortion, pneumonia, arthritis, and endometritis in cattle (Uematsu et al., 1989, Noakes et al., 1990, Carter and Chengappa, 1991, Semambo et al., 1991). Mastitis caused by *T. pyogenes* is reported to occur usually sporadically during dry period or early lactation, and in near 90% of cases, only one quarter is infected (Madsen et al., 1992a, Madsen et al., 1992b). In Europe, outbreaks may occur during summer. Transmission of *T. pyogenes* is associated with the activity of biting flies such as *Hydrotaea irritans* (Evenhuis, 1980, Sol, 1990). In one study in England, almost 60% of cows that developed summer mastitis were culled (Hillerton et al., 1987). In the study by Olde Riekerink et al. (2008) in Canada, *T. pyogenes* was isolated from 1.2 % of milk samples collected from CM cases in 106 dairy farms.

Gram negative bacteria

These bacteria are mostly isolated from acute CM in herds with low or high BMSCC (Barkema et al., 1998). Gram negative bacteria are classified as environmental pathogens, and their source is mainly bedding material, manure, soil, or other organic materials which can be found in the environment of cows (Smith and Hogan, 1993, Hogan and Smith, 2003).

Coliforms. The most common coliforms isolated from IMI cases are *E.coli* which are part of the normal flora of the cow's gastrointestinal tract. *Klebsiella* spp and *Enterobacter* are two other coliforms that reside in soil, grains, water, or gastrointestinal system of animals. In addition to mastitis these microorganisms may cause respiratory or urogenital infections (Hogan and Smith, 2003).

Coliforms usually invade the mammary gland by the teat canal, and their spread from other infected organs via vascular or lymphatic vessels rarely occurs. They multiply rapidly with or without adhesion. Coliforms are iron-dependant microorganisms and lactoferrin which binds iron and keeps it inaccessible to coliforms, has an inhibitory influence on coliform multiplication. Lactoferrin increases during dry period where mammary glands undergo involution. However, enterobactin iron acquisition system helps these bacteria overcome this defense mechanism. The main cellular mechanism against coliforms is phagocytosis by neutrophils. Susceptibility to phagocytosis is determined by surface antigens. Capsule producing strains of *E coli* are more resistant to defence mechanism in comparison with non-capsule producing strains. Thus, IMI induced by capsule producing strains tend to last longer. Endotoxin is the main virulence factor of gram negative bacteria. It consists of lipopolysaccharide constituents of the cell wall of the gram negative bacteria which is released after the bacterial death, and has the potential to induce a strong host inflammatory response (Fernandes et al., 2011).

Coliforms are the main etiological agent for CM in herds with good hygiene. Most clinical cases of coliform mastitis during the early lactating period originate from IMI acquired during the dry period. During lactation, coliform IMIs tend to be short term, and usually do not persist for more than 10 days. That is why the prevalence of this form of IMI is usually low. Coliforms IMI, however, are more prevalent immediately after calving (Hogan and Smith, 2003). In a cohort study in The Netherlands on 300 dairy herds it was concluded that 4.77% of all episodes of *E.coli* induced CM may become persistent infection (Dopfer et al., 1999). Coliform CM is often characterized by visible changes in milk and swollen udder. In a study by Hogan et al. (1989a) on low SCC dairy herds, 29% of coliform CM cases, were reported to be accompanied by systemic signs. In confinement systems, incidence of coliforms CM reaches its highest point during summer, while in dry lots and grazing systems, incidence is higher during rainy periods. The rate of gram negative induced CM is also higher in older cows. As a result, older cows calving in summer in confinement housing systems are at the greatest risk of getting coliform CM (Hogan and Smith, 2003).

Escherichia coli. In the study by Olde Riekerink et al. (2008) *E. coli* CM had highest incidence in herds with low to medium BMSCC and in dairy farms with free stall barns. In vivo studies demonstrated that all strains of *E coli* which may cause transient or persistent IMI adhere to mammary epithelial cell culture (MAC-T), but the strains associated with persistent IMI are more capable of invasion, survival, replication in cells, and adherence (Dogan et al., 2006). The risk of severe *E.coli* CM is higher if IMI occurs during the first three months after parturition (Lehtolainen et al., 2003). In a cohort study in The Netherlands on 300 dairy herds it was concluded that 4.77% of all episodes of *E.coli* induced CM may become persistent infection (Dopfer et al., 1999).

***Klebsiella* spp.** These bacteria are nonmotile, nonhemolytic, and capable of surviving in the presence of lactoferrin inhibitors in mammary glands. Two well-known species of this genus are associated with bovine mastitis: *K. oxytoca* and *K. pneumonia* (Todhunter et al., 1990, Schukken et al., 2012). Although *Klebsiella* spp are capable of proliferation in different bedding types and cow feces, saw dust used as bedding has been associated with higher risk of *Klebsiella* spp mastitis outbreaks compared to other bedding types (Hogan et al., 1989b). Similar to *E. coli*, *Klebsiella* spp. CM has higher incidence in low BMSCC herds and free stall barns (Olde Riekerink et al., 2008). However, some characteristics of *Klebsiella* spp. CM makes it more challenging to dairy producers compared to *E. coli* CM. For example, milk yield reduction caused by *Klebsiella* spp is more severe and last longer compared to milk loss induced by *E. coli* IMI (Godden et al., 2003). Moreover, *Klebsiella* spp. mastitis may show more severe clinical signs and usually show limited response to treatment (Smith and Hogan, 1993, Erskine et al., 2002, Roberson et al., 2004).

Coliform mastitis can be mitigated using vaccination with core antigen bacterin. In this type of vaccine, bacteria such as *E coli* J5 or *Salmonella typhimurium* Re17 are utilised (McClure et al., 1994). Using core antigen vaccines reduces mainly the severity of CM due to not only *E coli,* but also other gram negative bacteria such as *Klebsiella, Serratia*, *Pseudomonas,* and *Proteus* (Hogan et al., González et al., 1989). These vaccines decrease the bacterial count of infected quarters in IMI cases by 25%, and the duration of CM in vaccinated cows was reduced by 50% compared to non-vaccinated cows (Hogan et al., 1995). According to cost-benefit modeling, vaccination is an economically valuable strategy in well managed herds with coliform CM problem (Hogan and Smith, 2003).

Sporadic outbreaks of mastitis caused by non-coliform gram negative bacteria like *Serratia*, *Pseudomonas, Proteus* are reported, but CM due to these agents tend to occur less frequently with less severe clinical signs than CM caused by coliform agents (Hogan and Smith, 2003). Besides, these bacteria are likely to cause chronic mastitis that lasts several lactation cycles (Hogan et al., 1989a). Inorganic bedding material such as sand and crushed limestone may help reduce the incidence of gram negative CM. Organic bedding like wood shaving, sawdust, chopped newspaper, recycled manure, straw, and corn fodder maintain a large number of coliform bacteria (Hogan et al., 1989b).

Other mastitis pathogen agents

Mycoplasma spp. Mycoplasma spp are very small cell wall-less bacteria with a minuscule genome (Razin et al., 1998). Despite their limited genetic and metabolic capacity, *Mycoplasma* are recognized major pathogens in livestock production (Minion, 2002). They may cause or contribute to pneumonia, arthritis, mastitis, and urogenital diseases in cattle (Gonzalez et al., 1992, Adegboye et al., 1996, Hum et al., 2000, Maunsell et al., 2011). Variable surface lipoproteins (**Vsp**) are the immune system stimulator antigens of Mycoplasma. These lipoproteins are greatly variable and polymorphic (Le Grand et al., 1996). This diversity is an effective strategy for host adaptation and evading the immune system (Nussbaum et al., 2002). Most common Mycoplasma species in bovine mastitis are *M. bovis*, *M. californicum,* and *M. bovigenitalium* (Fox, 2012). Different features of Mycoplasma infection in calves such as otitis, arthritis and respiratory disease may be evident in herds involved with Mycoplasma mastitis, especially in farms where calves are fed unpasteurized milk (Butler et al., 2000). Asymptomatic carrier cows may shed *Mycoplasma* in milk, feces, nasal and vaginal discharge. In addition to cow-cow transmission, this bacteria is capable of internal (i.e. hematogenous or lymphatic spread) and vertical transmission (Fox, 2012).

Although some Mycoplasma IMI may be eliminated spontaneously, infections are generally considered permanent (Fox et al., 2005). Even if the milk bacteriological culture becomes negative after treatment, the bacteria may reside in some other organs of the cow with potential to re-infect the mammary gland later in time. Considering *Mycoplasma* IMI may become persistent and non-responding to antimicrobial treatments, identification of infected animals and isolation and culling are the main control strategies. Since *Mycoplasma* spp are susceptible to most disinfectants, meticulous hygiene during milking, particularly post milking asepsis, is an important measure to control transmission of this bacteria (González and Wilson, 2003, Punyapornwithaya et al., 2011).

Occasionally, yeasts such as Candida and Trichosporon spp (Hogan, 1999, Gonzalez et al., 2001) and Algae like Prototheca spp (Janosi et al., 2001, Marques et al., 2008) may also infect mammary glands.

1.5 Diagnosis

Detecting inflammation

When mastitis is not clinically detectable, direct and indirect measurement of the cells aggregated in milk is a common way of detecting the inflammation due to IMI. The milk secreted by healthy quarters contains some somatic cells including macrophages (60%), lymphocytes (25%), and polymorphonuclear leukocytes (15%) (Burvenich et al., 1995, Kelly et al., 2000). Leukocytes, mainly neutrophils, aggregate in the mammary glands and milk as a consequence of infection and chemotaxis. The somatic cells released in the milk of infected quarter are mainly leukocytes (99%), remaining cells are sloughed epithelial cells of the mammary gland (1%) (Pillai et al., 2001). Direct cell counting of milk sample (i.e. somatic cells count (**SCC**)) can be used to monitor general herd udder health and to identify cows or quarters that require further diagnostic tests such as milk bacteriological culture (Schukken et al., 2003). Parity, the stage of lactation, and amount of milk production can also influence SCC. During periparturient and dry period, SCC is usually higher due either to the lower milk yield or the higher probability of IMI in that stages of the production cycle. Any diseases that cause reduction in milk yield can lead to an increase of SCC as a result of somatic cells being concentrated in a smaller volume of milk. In addition, older cows usually produce milk with higher SCC which could be associated with their higher prevalence of IMI. However, during the peak of milk yield until mid-lactation, SCC is at its lowest.

Ali and Shook (1980) described a method to calculate Somatic Cell Score (**SCS**), which is a log transformation of SCC used to facilitate the interpretation of SCC. Somatic cell score can be computed using formula 1.

$$SCS = \log_2\left(\frac{SCC}{100}\right) + 3$$

Formula 1

Where SCC is reported in x1,000 cells/ml. The advantages of using SCS in statistical analyses are that there is a linear correlation between milk production and SCS. It also has higher heritability, symmetrical distribution, constant variance, and its mean is close to the median. This measure is, therefore, often used in place of SCC.

When SCC increases as a consequence of IMI, then it does not get back to pre-infection SCC until all pathogenic microorganisms are eliminated which may take few weeks (Werven et al., 1997). Somatic cell count is performed by means of direct microscopic examination, or by equipments like coulter counter or fluoro-opto-electronics. During the course of an IMI, some variations in SCC may be seen. These variations can be associated with cycles of multiplications and elimination of the pathogens. Because of these variations of SCC, the final decision for the animal or the quarter should not be made on one single test (Schepers et al., 1997, Schukken et al., 2003).

One of the rapid inexpensive tests to diagnose mastitis is California Mastitis Test (**CMT**), which can be performed in farm (cow-side). A paddle with four cups is used in CMT to help evaluate the collected milk samples from quarters separately. However, this test can also be conducted using composite milk samples. California Mastitis Test is an indirect semi-quantitative measurement of somatic cells in milk samples. The reagent added to milk sample in CMT contains both a detergent and bromcresol purple as pH indicator. Equal amounts of milk and reagent are poured in each cup and mixed by rotating the CMT paddle. Somatic cells in the milk are lysed by the detergent and following reaction between the reagent and nucleotide acids of lysed cells, the mixture turned into gel. The higher number of somatic cells in the milk sample, the firmer the formed gel would be in the cup. Therefore, a score is assigned to the mixture of each cup based on the consistency and gel formation in the mixture (Schalm and Noorlander, 1957, Hogan JS, 1999, Pyörälä, 2003) (Tableau IV).

Table IV. Estimated somatic cell levels associated with CMT scores- reproduced from Hogan (1999)

CMT score	**Relative range of somatic cell level ×1000 cells/mL**
Negative	<200
Trace (suspicious)	150 – 500
1 (suspicious)	400 – 1,500
2 (positive)	800 – 5,000
3 (positive)	>5,000

Reported sensitivity and specificity of CMT are variable based on lactation stage of the cow. In the study by Roy et. al. (2009) sensitivity and specificity of CMT for identifying major pathogens IMI two weeks before parturition at quarter level were reported at 79% and 58%, respectively. It was concluded in the latter study that CMT is not a reliable test for IMI in pre-calving period particularly when both major and minor pathogens are sought. However, in Roy et. al. (2009) CMT was suggested to be used to identify heifers that are not infected in pre-calving time since the negative predictive value of CMT was high for major pathogens at quarter level. In another study, sensitivity and specificity of CMT for detecting major pathogen IMIs in the first week of lactation were reported at 82.4% and 80.6%, respectively

(Dingwell et al., 2003). Being rapid, low priced, and feasible in farm by farm staff, this test is still popular among producers for SCM screening.

Detecting pathogens

In order to identify the etiologic agent of mastitis, additional tests on aseptically collected milk samples are required. On many occasions, bacteriological culture is first realized followed by various biochemical tests based on phenotypic methods that allow identification of the microorganism based on its morphology or ability to metabolise a specific substrate. Bacteriological culture is widely used for IMI diagnosis using milk samples in many studies, but cannot be considered a gold-standard test. (Hogan JS, 1999, Britten, 2012). Being rather low priced, phenotypic methods are very popular; however, the risk of false negatives in no-growth results remains a noticeable challenge for these methods. Therefore, genotypic methods (e g., PCR) are used as complementary tests detecting specific DNA sequences in microorganism genomes. Genotypic methods are highly sensitive, and detect microorganisms despite being in very low numbers, nonviable , or incapable of growth (Duarte et al., 2015).

Milk samples of individual cows submitted for bacteriological culture may be collected from a single quarter (quarter sample), or as a pool of all functional quarters (composite sample). Taking composite sample reduces the costs of diagnosis, but may increase the risk of false negative result if IMI is due to some pathogens (e.g., *S.aureus* and *Mycoplasma* spp.) that shed few bacteria (Reyher and Dohoo, 2011). This diagnostic approach can provide evidence for presence of bacteria and type of predominant agent. If contagious agents are isolated in culture (*S.aureus, S. agalactiae, Mycoplasma* spp.), presence of these IMI in the herd is confirmed. However, negative culture results for contagious agents does not necessarily mean that these IMI are not present in the herd. Isolated coliforms and environmental streptococci can originate from IMI or from a contamination of the milk during sample collection procedure. Counting colony forming units per millilitre is a semi-quantitative measurement of milk sample bacterial load. General isolation media (e.g. blood agar) are used to estimate total growth, and more specific media are sometimes used to identify the bacterial groups such as gram negative, coliforms, streptococci, and staphylococci. Bacteriological culture is followed by biochemical tests to identify the bacterial colonies retrieved.

Accuracy of test varies between different types of pathogen. For example, sensitivity and specificity of bacteriological culture for isolation of *S. aureus* were reported at 91-100% and 97.6-100%, respectively (Buelow et al., 1996). However, a major concern with bacteriological culture of single milk samples is that 26 to 50% of samples collected from CM or SCM are culture negative (Makovec and Ruegg, 2003, Olde Riekerink et al., 2008, Taponen et al., 2009). Some culture negative samples were shown to contain several species of common pathogens even in large numbers (Bexiga et al., 2011). Some studies tried to increase the accuracy of this test by conducting repeated sampling. For example, consensual gold standard definitions were proposed by Andersen et al. (2010) for bacteriological culture procedures based on triplicate samples. In that study, it was proposed that isolation of a specific pathogen from two or three samples among triplicate milk samples collected at three-day intervals or isolation of a specific pathogen on one sampling but with >1,000 cfu/mL milk (at least 10 colonies) should be considered indicative of an IMI.

More recently, on-farm milk culture using selective media has been proposed for mastitis diagnostic. Although using on-farm culturing could increase the speed of process, accuracy may be reduced to 80% compared to bacteriological culture conducted in a laboratory (Pol et al., 2009). Milk samples can also be collected from bulk tank milk and submitted for bacteriological analyses to determined herd IMI status. This can be performed using conventional bacteriological culture and colony counting or automated enumeration of bacteria. Bulk tank milk bacterial count is one of the criteria used to evaluate in milk quality premium programs (Smith, 2014).

When conventional bacteriological culture gives negative results or when minor pathogens are isolated from a milk sample with high SCC, other complementary tests with higher sensitivity can be used. For example, in one study real-time PCR-based tests identified pathogens in 47% of milk samples that were already diagnosed culture negative (Bexiga et al., 2011) .

1.6 Negative impacts associated with mastitis

Negative impacts associated with CM

Clinical mastitis is associated with economic consequences due to reduced milk production, discarded milk, use of diagnostic tests, medications and the extra labor required for treatment, veterinarian fees, increase risk of culling and mortality, and change in milk composition and quality.

Mild yield reduction following CM. Some studies estimated the amount of milk yield reduction due to CM in the lactation of an affected cow as absolute values (in kg), and as function of cow's parity (primiparous vs. multiparous), cow's CM episode number (first episode in a lactation vs. subsequent episodes), and pathogen involved (Gröhn et al., 2004, Hertl et al., 2014b). The influence of first case CM induced by gram negative, gram positive, and other bacteria on lactation curve of primiparous cows are depicted in Figure 5. One of the disadvantages of estimating an absolute value for milk yield reduction following CM is that cow milk production before developing CM is not taken into account. Therefore, estimated milk loss for both high and low producing cows with similar parity, number of CM episode, and isolated pathogens would be considered equal.

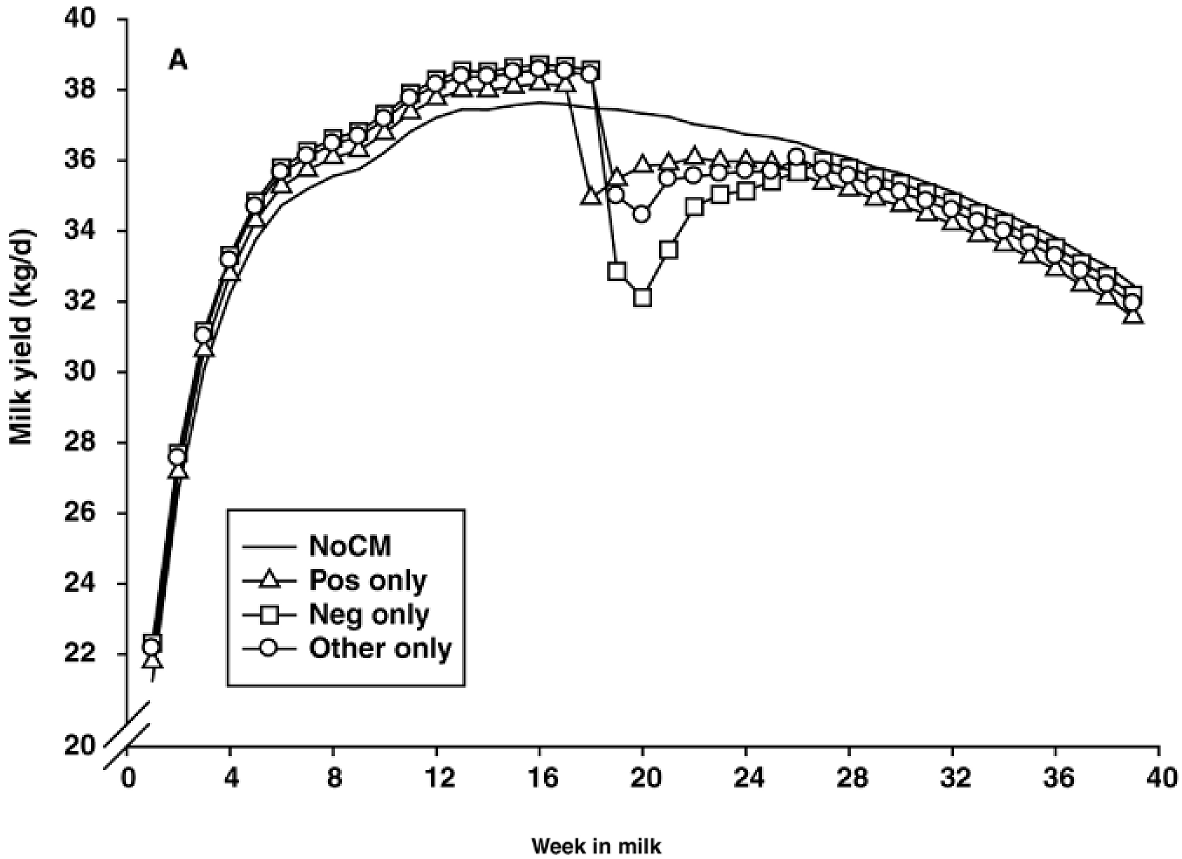

Figure 5. Lactation curve for primiparous cows without CM (NoCM), and first case of gram positive (Pos only), gram negative (Neg only), or other (Other only) CM; reproduced from Schukken et al. (2009)

That is why some other studies estimated the milk yield reduction as a proportion of cow milk production. For example, relative milk loss was estimated to vary between 8% loss (if CM occurred in the first month of lactation) and 1% (if CM occurred in the ninth month of lactation) (Huijps et al., 2008b). On average, a 5% loss in milk production was reported for the remainder of the lactation following CM (Seegers et al., 2003b). The distribution of CM occurring in the first month of lactation was reported to be 30% of total herd CM cases. (de Haas et al., 2002). Occurrence of CM in this period resulted in most severe reductions in milk yield. Average milk loss, in a complete lactation, as a result of an early lactation CM has been reported to be 911 kg (Lescourret and Coulon, 1994).

The pattern of milk loss was also studied. Older cows that developed CM showed more dramatic milk yield reduction compared to heifers that experienced CM. Milk yield reduction usually began several weeks before the CM diagnosis. Reduction in milk yield was highest in the first week of diagnosis, and then tapered for near two months; however, minor milk loss could be evident even in the subsequent lactation, so cows experiencing CM never fully recover to their potential production level. In addition, Higher milk production is recognized as a risk factor for CM. Therefore, high producing cows are more susceptible to CM (Peeler et al., 2000, O'Reilly et al., 2006, Bar et al., 2007). In a study by Gröhn (2004) the amount of reduction in milk yield due to CM was calculated considering the interaction of cow's parity and isolated pathogens. It was demonstrated that in first lactation, highest milk yield drops were evident in CM cases with milk samples from which *S. aureus, E. coli* or *Klebsiella* spp. were isolated. While, in second lactation *Streptococcus* spp, *S. aureus, E. coli* or *Klebsiella* spp, and *Trueperella pyogenes* caused the largest reduction in milk yield. Milk losses also occurred in CM cases with no isolated bacteria.

The quantity of milk yield reduction is also influenced by treatment protocol. In CM cases that receive supportive treatments (i.e. oxytocine and flunixine meglumine) without antibiotic, the volume of milk yield reduction in whole lactation can be up to three times higher than milk yield reduction of CM cases with similar mastitis severity score that were treated by antibiotics in addition to supportive treatments (Shim et al., 2004).

Milk discarded due to CM. Milk produced by cows that are experiencing CM is improper for human consumption and need to be discarded. The number of days for which milk is discarded depends on treatment duration and drug withdrawal time in cases that are treated, or on time for return of milk to normal appearance, in cases that are not treated. In the economic model by Huijps et al. (2008b), the typical duration of discarding milk of treated CM cases was considered 6 days (3 days treatment + 3 days withdrawal time). In some dairy herds, non-salable milk is used as an input, mainly to feed calves (Vasseur et al., 2010), in order to help mitigate a part of losses due to the discarded milk. This practice, however, is known to increase risk of disease transmission and antibiotic resistance, despite waste milk pasteurization, and should, therefore, be discouraged (Wray et al., 1990, Aust et al., 2013, Brunton et al., 2014).

Diagnostic tests due to CM. Diagnosis of CM is often based on detection of clinical features (i.e. abnormal milk, swollen udder, or sick cow). Examining foremilk by using a strip cup or plate before attaching milking unit is an important practice to monitor milk appearance and helps detect abnormalities. However, producers and veterinarians may use diagnostic tests to monitor fresh cows and detect CM earlier particularly in valuable cows. In addition, some diagnostic tests such as bacteriological culture may be used to identify the etiologic agents of CM and their antibiotic susceptibility to establish an effective protocol for subsequent treatments (Sears and McCarthy, 2003a).

Drugs usage due to CM. To reduce recovery time from IMI and return to milk production, antimicrobials are administered to CM cases via intramammary or systemic routes. Moreover, pain due to mastitis should be controlled to fulfill the standards for cow welfare. In Canada 98% of herds were reporting using intramammary antibiotic infusion to treat CM, and penicillin combination products were the most commonly used product for this purpose followed by penicillins, first generation cephalosporins, and lincosamides (Saini et al., 2012). In the US, nearly 80% of mild CM cases were treated with only intramammary antibiotic. Ceftiofur and cephapirin were reported to be the most common intramammary antibiotics used in the US to treat CM. These were usually administered for 4-6 days (Oliveira and Ruegg, 2014).

Veterinary services due to CM. The proportion of CM cases visited and treated by veterinarians varies based on country regulations. For example, in Sweden and Finland, antibiotic administration for CM treatment can solely be performed by veterinarians, and treatments should be reported to animal disease recording system organizations (Emanuelson, 1988, Heikkila et al., 2012). However, in Canada, CM cases may be treated by producers or veterinarians (Saini et al., 2012). In countries where farm personnel treat CM, extra labor is required from farm personnel for CM treatment (Bar et al., 2008b). Overall time needed for treating a CM case was assumed to be 45 minutes in Huijps et al. (2008a).

Culling and mortality due to CM. Although most culling decision are based on a combination of factors (Fetrow et al., 2006), the risk of culling is increased in cows that develop mastitis. In a study in the US, among nine possible disposal codes, mastitis and production reduction accounted for 12 % of all culling decisions reported by producers

(Pinedo et al., 2010). In Grohn et al. (2005), the hazard ratio of culling was estimated highest if CM was diagnosed in third to fifth month of the lactation. The association between CM and risk of culling was demonstrated with CM induced by different pathogens. However, hazard ratio of culling was particularly high in *Staphylococcus* spp, *E. coli, Klebsiella*, and *T. pyogenes* CM. Clinical mastitis is also demonstrated to be associated with odds of mortality (McConnel et al., 2015). The odds ratio of mortality was reported highest in second CM episode in multiparous cows (Bar et al., 2008a). In the study by Cha et al. (2013), the influence of type of pathogens isolated, cow parity, and CM episode number on risk of culling and mortality were analyzed altogether, and risk ratios of culling or mortality were reported to vary between 3.1 and 10.4 in different CM scenarios.

Effects of CM on reproduction. In a study by Schrick et al. (2001) it was demonstrated that cows experiencing CM had 143±8.5 higher days open and 3±0.2 more number of services per conception. To determine whether a causal relationship truly exist between CM and fertility, additional studies repeating these results would be needed.

Negative impacts associated with SCM

Economic consequences of SCM could be due to reduced milk yield, change in milk composition and quality, penalty payment, loss of premium, discarding milk, diagnosis, treatment, veterinary consult, lower reproductive performance, and culling.

Milk yield reduction due to SCM. Milk production loss constitute the highest economic costs compared to other consequences of mastitis (Huijps et al., 2008b). The amount of reduction in milk yield, as a consequence of IMI, is closely related to the natural logarithm of SCC. This association is affected by the cow breed, parity, and stage of lactation. Estimated quantity of milk yield reduction as a function of SCC increase varied among different studies (Hortet et al., 1999, Koldeweij et al., 1999, Seegers et al., 2003b). However, the dilution effect was later introduced to cause an overestimation of milk yield reduction in prior studies (Green et al., 2006). Because of the dilution effect, in high producing cows, SCC measurement is biased and results of daily tests are lower than the real SCC; therefore, SCC should be justified for dilution effect before measuring the association between SCC and milk yield reduction. The adjusted SCC was used in Halasa et al. (2009), in which milk yield was predicted to reduce 0.28 and 0.50 kg/day in primiparous and multiparous cow with test day SCC of 200,000 cells/mL, respectively.

The study by Fetrow et al. (1991) demonstrated that SCM has also negative impacts on milk production of the cow in the subsequent lactation which is called “carry-over effect”; however, the estimated effect was quite limited in that latter study and it is not usually taken into consideration in economic models. Histopathologic studies have demonstrated proliferation of fibrous tissue in mammary glands affected by mastitis (Benites et al., 2002). The appearance of fibrous tissue that replace the epithelial cells in the alveoli could be one of the reasons that cow milk production does not get back to the pre-mastitis level even in subsequent lactations (Petrovski, 2006).

The analysis of economic loss due to reduced milk yield in regions where quota system is adopted including European Union (prior to 2015), Norway, and Canada, is different from other countries without that system. If the regulation allows leasing out the quota, then in case of reduced milk production, the farmer may compensate the lower revenue by such ways (Halasa et al., 2007a).

Reduced milk quality due to SCM. Mastitis has remarkable effects on raw milk quality which determines the pasteurized milk shelf life. Some factors including SCC, bacterial count, and antibiotic residues are used to determine whether milk is entitled to penalty or premium in dairy companies. Therefore, these milk quality factors have direct correlation with economic losses (Halasa et al., 2007a). The higher SCC and bacterial count are in raw milk, the higher the concentration of heat resistant protease will be. These enzymes have the potential to break down casein and decrease the pasteurized milk shelf life (Verdi and Barbano, 1988, Barbano et al., 2006). In addition to fluid milk, the quality of other dairy products is influenced by high SCC level. Dairy products (cheese, yogurt, butter, and ice-cream) use 71% of the Canadian milk production (Canadian Dairy Commission, 2016b).

Discarded milk due to SCM. As a consequence of SCM, milk maybe discarded. The reasons for this practice include high SCC, high bacterial count, or antibiotic residues during withdrawal time following drug administration to treat SCM (Halasa et al., 2007a). However, it is important to note that treating SCM during the lactating period is not as common as treating CM. Some of the discarde milk is sometimes use as feed for young calves, rather than completely being thrown away.

Veterinary services for SCM. Dairy producers consult veterinary practitioners or dairy advisors regarding SCM and herd BMSCC management (Lam et al., 2011). Perception of herd mastitis problem that requires professional intervention varies among producers. However, dairy farmers reported that the local veterinarian is the first they would contact if mastitis problem is perceived in the herd (Jansen et al., 2009). Rodriguez et al. (2005) showed that herds with high BMSCC reported a lower frequency of consultation with a professional about milk quality and udder health. Moreover, in the study of Gill et al. (1990a) regular udder health visits was shown to be associated with lower SCS.

Diagnosis of SCM. Subclinical mastitis detection in herd is more challenging than CM as the cases do not show clinical changes. Less expensive tests capable of detecting inflammation in the quarter such as CMT or SCC are commonly used for screening. Then, bacteriological culture are conducted in subsequent steps to identify pathogens in selected individual cows (Pyörälä, 2003). Odds of SCM is shown to be lower in herds that regularly conduct CMT for screening (Busato et al., 2000).

Treatment of SCM. Subclinical mastitis is not usually treated during lactation unless it turns into CM. One of the reasons for producers' reluctance to treat SCM during lactation is low response to treatment in that period and the important amount of milk discarded (Deluyker et al., 2005). There is a study showing that treatment of *S. aureus* SCM during lactation could be beneficial because of prevention of flare-up and pathogen transmission in herd; however, the economic impact of treatment highly depends on characteristics of the cow and herd (Swinkels et al., 2005).

Effects of SCM on reproduction. Mastitis may have negative impacts on other organs' functions. Risk of reduced fertility due to mastitis have been studied. Schrick et al. (2001) demonstrated that in cows affected by CM or SCM before first service, reproductive performance was reduced. Zootechnical markers such as number of services by conception, time to first service, and number of days open were all increased in cows experiencing SCM compared to control cows.

Culling due to SCM. Cows that develop SCM have a higher risk to be culled compared to other herd mates. A significant correlation is demonstrated between sire predicted transmitting ability for SCS and the length of productive life of their daughters (Cranford and Pearson, 2001). Caraviello et al. (2005) showed that risk of culling in high SCC (>700,000 cells/mL) cows is higher than low SCC cows (200,000 to 250,000 cells/mL). In this latter study, estimated risk of culling in high SCC cows was 3.4, 2.7, and 2.3 times higher than low SCC cows in herds with low, medium, and high average SCC, respectively.

1.7 Mastitis control programs

The management practices used to minimize the risk of new IMI and persistency of infections are critical for the dairy industry. The five-point plan was first presented by the National Institute for Research into Dairying in UK based on some controlled studies in dairy farms (Dodd et al., 1969, Neave et al., 1969). This program aimed mostly at limiting the transmission of contagious pathogens (Table IV). This program was later modified into the ten-point mastitis control plan recommended by the National Mastitis Council (**NMC**), in which some additional practices were added to control environmental agent as well (National Mastitis Council Research Committee).

In order to reduce prevalence of mastitis in herd, efforts should be on both preventing new infection development or shortening the IMI duration. New infection is influenced by the probability of healthy cow being exposed to pathogens (i.e. bacterial transmission due to contact with sub-clinically infected cows or due to the environment). The IMI persistency is associated with host and pathogen characteristics, treatment efficiency, and producer`s culling decisions.

Implementing mastitis control programs requires hard work. The goals should be to keep the team motivated and to encourage the staff to keep the standards. One important strategy is to control the bacterial population in the cows' environment since it is associated with the bacterial density on teat skin and with CM incidence (Zdanowicz et al., 2004, Dohmen et al., 2010). Cow cleanliness, especially cleanliness of the udder and hind leg regions, is also significantly correlated with SCC and IMI incidence (Reneau et al., 2005, Dohmen et al., 2010, de Pinho Manzi et al., 2012). Strict hygiene during milking through practices such as wearing gloves, using individual towels to dry the teats (Huijps et al., 2010), and teat disinfection is significantly associated with lower SCC as well (Barnouin et al., 2004, Dufour et al., 2011). Milking equipment should be monitored regularly as malfunctioning milking facilities may severely affect teat ends and compromise the local defence mechanisms (Rasmussen et al., 1994).

Diligent record keeping is required to regularly monitor cows' production and udder health. Blanket dry cow therapy (Dufour et al., 2011), efficient CM treatment, isolation and culling of chronic mastitis cases, are recommended to eliminate existing IMI and to reduce the exposure of non-infected cows to contagious agents (Wilson et al., 1995, Zecconi et al., 2003). Implemented mastitis control program should be regularly revised. Not all farmers adopt all these mastitis control measures. One of the most significant inhibitory factors is financial limitations, and the fact that farmers are not convinced that these techniques are efficient enough to be worth the investment.

Table V. Comparison of two mastitis control program- Adapted from NMC research committee and Radostits (2007)

Five-point plan	Ten-point plan
1. Post-milking teat disinfection 2. Total dry cow therapy 3. Treatment of clinical cases during lactation 4. Proper maintenance of the milking equipment 5. Culling chronically infected cows	1. Establishment of goals for udder health 2. Maintenance of a clean, dry, comfortable environment 3. Proper milking procedure 4. Proper maintenance and use of milking equipment 5. Good record keeping 6. Appropriate management of clinical mastitis during lactation 7. Effective dry cow management 8. Maintenance of biosecurity for contagious pathogens and marketing of chronically infected cows 9. Regular monitoring of udder health status 10. Periodic review of mastitis control program

2. Modelling costs of mastitis

2.1 Economic models that can be used to evaluate costs of diseases

Economic models are tools to describe the interrelationships among selected variables in an economic reality by mathematical techniques. In animal health economics, there are different models used to support the producer decision-making process. There are four important characteristics that distinguish different models. The first is the modelling approach. Some models use epidemiological descriptive data (i.e. positive approach that is used in empirical models), while other models use computer simulation techniques (i.e. normative approach which is used in mechanical models). The second is optimization. Models that use optimization seek the optimal solution in terms of cost-efficiency with regard to objective function and restrictions, whereas in simulation models, outcomes are calculated based on input variables. The third characteristic is dynamicity. Dynamic models take the variable of time into account, and can be used to simulate a system behavior over time; whereas, other models that do not consider time are called static models. The fourth is stochasticity. Stochastic models take the factor of uncertainty into account by using probability distributions or randomness, while deterministic models predict definite values. (Dijkhuizen and Morris, 1997).

In following paragraphs, some basic and commonly used models in animal health economics are briefly explained. These models may be used solely or in combination with other models.

Budgeting

By using budgeting models, profitability of farm production can be estimated with consideration of a disease control strategy. Since profit is calculated by subtracting expenses from revenue, there are two ways of increasing the profit; either by increasing production efficiency, or by decreasing costs of production. "Partial budgeting" is a modified form of budgeting to evaluate the effectiveness of small scale interventions in overall profitability of the production during a restricted period of time. In partial budgeting, only the revenues and costs related to the intervention of interest are evaluated; therefore, this is a rather rapid and simple process compared to comprehensive budgeting (Marsh, 1999).

Decision tree analysis

In a decision tree analysis, the flow of events is depicted using nodes and branches in chronological order with probability associated with each outcome. An important feature of this analysis is that it takes the factor of uncertainty into account; therefore, it can be useful in animal health economics. In order to prepare a decision tree, a complete list of mutually exclusive events should be prepared first.

Cost-benefit analysis

This model is generally used to evaluate economic consequences of adopting new strategies which are associated with control of a disease in a longer period of time (5 to 20 years). While this method is commonly used to support decisions at large scales such as eradicating a disease at national level, it can also be used for animal health decisions at farm level. The applied method is close to budgeting, and is performed by identifying flow of costs, flow of returns, discount rate, and decision criteria.

2.2 Models used for mastitis

The studies investigating economics of mastitis were usually focused on a limited part of mastitis consequences. For example, decision making process regarding a control measure, or estimating value of one cost component (e.g., milk production loss) or one category (e.g., CM). There was only one comprehensive study conducted by van Soest et al. (2016a) in The Netherlands covering costs attributed to all components of CM, SCM, and preventive measure. In the latter study, costs attributed to CM and SCM were estimated by the economic model developed by Huijps et al. (2008b). Then, prevention cost was estimated based on assumed values of required labor and materials for preventive measures. Finally, mastitis cost was predicted for different scenarios with low vs. high milk price and low vs. high labor cost.

Rollin et al. (2015) used deterministic partial budget model to investigate costs of CM occurring in the first month of lactation in the US. The opportunities to mitigate a part of the estimated mastitis cost by management practices were evaluated. Dynamic optimization and simulation modelling was used in another study in the US to estimate costs of mastitis in three mastitis categories, gram positive, gram negative, and other pathogens. Based on cost of each mastitis type, optimal decisions on treatment and culling of infected cows were discussed (Cha et al., 2011). In the study by Huijps et al. (2009), Stochastic models were used to estimate cost of mastitis in heifers in early lactation, and the variation this estimated cost was analysed in

Dutch and Belgian dairy herds by taking into account the factor of uncertainty. Important factors that were considered in the latter study included minimum, maximum, and most likely probability of mastitis occurrence in a heifer, production loss percentage, probability of mastitis treatment, and probability of culling infected heifers.

In the study of Berry et al. (2004) decision tree analysis was used to evaluate producer's decision for dry cow therapy at cow level and possible economic outcomes of such a decision. Cow udder status, isolated pathogen, and the product used at dry off (internal teat sealant vs. antibiotic) were the main variables, in this analysis, that influenced the economic outcome. In the study by Beck et al. (1992) conducted in the UK, cost-benefit analysis of mastitis control measures was performed. It was demonstrated that there was substantial profit for producers in adopting major mastitis control measures (dry cow therapy and teat disinfection) because the economic value of reduced mastitis incidence was far beyond the cost of implementing these practices. In another study by McNab and Meek (1991) in Canada, dry cow therapy was analysed using the same approach. Yalçin and Stott (2000) studied the benefits of some management practices by means of a stochastic dynamic model. This model was used to compare the probability of involuntary culling in different scenarios of adopting mastitis control measures (e.g., adopting dry cow therapy only or all preventive measures).

In addition to these mentioned examples, many other studies used different modeling types to investigate mastitis economic aspects. The inputs used for the models were mainly from literature, producer reports, or expert opinions. The quality of input values is a critical factor in these analyses (Marsh, 1999). Through current regular monitoring plans, such as DHI programs, collecting records on udder health is facilitated, and these valuable databases could be used for conducting economic studies.

Chapter 2 - Mastitis-associated costs on Canadian dairy farms

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2.1 ABSTRACT

Mastitis imposes considerable and recurring economic losses on the dairy industry worldwide. The main objective of this study was to estimate the costs incurred by expenditures and production losses associated with mastitis on Canadian dairy farms in 2015, based on producer reports. Previously, published mastitis economic frameworks were used to develop an economic model with the most important cost components. Components investigated were divided between clinical mastitis (CM), subclinical mastitis (SCM), and other costs components (i.e., preventive measures and product quality). A questionnaire was mailed to 374 dairy producers randomly selected from the Canadian National Dairy Study 2015 to collect data on these costs components, and 145 dairy producers returned a completed questionnaire. For each herd, costs due to the different mastitis-related components were computed by applying the values reported by the dairy producer to the developed economic model. Then, for each herd, a proportion of the costs attributable to a specific component was computed by dividing absolute costs for this component by total herd mastitis-related costs. Median self-reported CM incidence was 19 cases/100 cow-years and mean self-reported bulk milk somatic cell count was 184,000 cells/mL. Most producers reported using post-milking teat disinfection (97%) and dry cow therapy (93%), and a substantial proportion of producers reported using pre-milking teat disinfection (79%) and wearing gloves during milking (77%). Mastitis costs were substantial (662 CAD/milking cow-year for a typical Canadian dairy farm), with a large portion of the costs (48%) being attributed to SCM, and 34% and 15% due to CM and implementation of preventive measures, respectively. For SCM, the two most important cost components were the subsequent milk yield reduction and culling (72% and 25% of SCM costs, respectively). For CM, first, second, and third most important cost components were culling (48% of CM costs), milk yield reduction following the CM events (34%), and discarded milk (11%), respectively. This study is the first since 1990 to investigate costs of mastitis in Canada. The figures obtained in the current study can be used to develop an economic model to compute mastitis costs at the herd and national level in Canada.

Keywords: dairy cow, mastitis, economic, Canada

2.2 INTRODUCTION

Mastitis imposes considerable economic losses on the dairy industry all over the world. This economic burden is due to the additional expenditures on mastitis prevention and treatment, and to the losses due to reduced milk production, culling and discarded milk. Altogether, these mastitis-related expenditures and production losses constitute the basic components of the mastitis economic model proposed by Halasa et al. (2007c). For instance, cows affected with mastitis may produce less milk and infected quarters may produce poor quality or even inconsumable milk that needs to be discarded. Furthermore, clinical mastitis (CM) needs to be detected and treated by the farm staff, which requires time and drugs. Sometimes, more complicated mastitis issues may require the intervention of a veterinarian. In case of inappropriate respond to the treatment, or in case of chronic untreatable and contagious infections, the cow may be culled from the herd and replaced by a healthy cow. In addition, preventive measures are increasingly adopted by producers to help improve udder health during both lactation and dry periods (Dufour et al., 2010).

In the framework proposed by Halasa et al. (2007c), reduction in milk production following CM or due to elevated SCC is an important component of the costs. Therefore, many studies have developed models to estimate the impact of high SCC or of pathogen-specific CM on subsequent milk production (Gröhn et al., 2005, Halasa et al., 2009, Hertl et al., 2014b). These models are of great help to estimate the amount of milk not produced following mastitis and associated costs, and could certainly be used in different countries and settings.

However, other components (e.g., cost of drugs, labor, materials and investments) may vary among countries and are influenced by factors such as resource prices, cost of milk production, policies controlling the dairy market, and producers' preferences for adopting prevention measures. For these reasons, studies on mastitis cost estimation should be conducted based on source populations restricted to a single geographical region such as a country or even a state (Weigler et al., 1990, Seegers et al., 2003a, Pérez-Cabal et al., 2008).

Only one study investigated some of the mastitis-related expenditures on Canadian dairy farms (Gill et al., 1990a). In this study, adoption proportion, cost, and efficiency of the practices included in the five-point plan to control contagious mastitis were investigated (Neave et al., 1969). Since the nineties, many other udder health-related practices have become common practices in Canadian dairy herds. Moreover, some expenses typical of modern dairy farms were not included in the initial economic model proposed by Halasa et al. (2007c). For example, over 80% of Canadian dairy producers participate in regular DHI programs. Since DHI programs are commonly used for udder health monitoring using SCC measurements, this expense should, perhaps, also be considered as a mastitis cost.

The objectives of the current study were to estimate the cost of mastitis on Canadian dairies and to investigate how the cost is distributed across the different cost components using an economic model derived from the Halasa et al. (2007) model. This study is the first part of a project aiming at investigating mastitis cost at the national level and to describe cost fluctuations over time.

2.3 MATERIALS AND METHODS

Economic Framework

For the current study, the mastitis economic framework proposed by Halasa et al. (2007c) was used as a foundation. A cross-sectional study (described below) was designed to collect data on factors previously identified in the latter study to have an impact on mastitis cost. Selected factors were those associated with current expenditures for mastitis treatment and control and mastitis-associated output losses (e.g., culling, discarded milk, reduced milk yield) which could be readily estimated by dairy producers, and included factors related to: drugs, discarded milk, veterinary services, labor, product quality, diagnostic, culling, materials and investments. Among components in the framework proposed by Halasa et al. (2007c), the increased risk of other diseases following CM was not included in this study since the causal association between CM and other health problems is not well demonstrated and reverse causation cannot be excluded. Although several studies provided evidence for effects of mastitis on reproductive efficiency (Plaizier et al., 1997, Santos et al., 2004, Hertl et al., 2014a), no consensus was found among these studies regarding its precise effect and subsequent economic impacts. For each cost component, equations were formulated to estimate the cost over a year for a given herd. Details regarding computation of the different cost components are given in the following sections. An exhaustive list of the equations used is presented in Appendix A.

Milk yield reduction. Reduced milk yield following a CM case was estimated using the results of the study by Seegers et al. (2003a) reporting that a cow experiencing CM produced 5% less milk in her whole lactation (regardless of parity, isolated pathogen, and new versus repeated nature of the CM case). In order to estimate the overall milk production loss due to subclinical mastitis (SCM) the model suggested by Fetrow et al. (1988) was used. In this model, a reduction of 190 kg of milk per milking cow is assumed for every one unit increase in the herd average linear score.

Drugs. Treatment of SCM during lactation was considered to be inefficient and not cost-effective for many years (Fox and Gay, 1993, Allore et al., 1998). However, more recent studies demonstrated that in many situations, treatment of SCM during the lactation could be beneficial from both economic and udder health point of view (Deluyker et al., 2005, Swinkels et al., 2005, Roy and Keefe, 2012). Because of concerns regarding economic efficiency of SCM treatment during lactation and risk of antimicrobial residues (National Mastitis Council, 2006, Green et al., 2008), treatment of SCM during the milking period is not systemically applied. Although application of SCM treatment during lactation varies among provinces, it is not as common as treatment of CM or dry cow therapy. Therefore, apart from dry cow treatment, we assumed that drugs were not used for the treatment of SCM during the lactation (assumption #1). Furthermore, therapeutic protocols are often selected based on severity of clinical signs, and on many farms, not all CM cases are treated. Different treatment protocols were, therefore, considered to be used for mild and moderate CM (i.e., abnormal milk with or without abnormal quarter appearance, but without systematic signs) compared to severe CM (i.e., systemic clinical signs) (Sears and McCarthy, 2003b). Mild and moderate CM, when treated, were assumed to be treated solely with intramammary antimicrobials. For treatment of severe CM, producers commonly also treat with systemic antimicrobials and anti-inflammatory drugs in addition to the usual intramammary treatment. We assumed that the most common treatment for severe CM would consist, in addition to local treatment, of a 3-d administration of systemic antimicrobials plus one dose of a nonsteroidal anti-inflammatory drug.

Consequently, to estimate costs for drugs used for CM treatment, we took into account for each farm the number of CM cases over a year, the proportion of severe cases, the proportion of mild and moderate CM cases that were treated, the mean number of days a case was treated, the frequency of drug administrations per day, and drugs' costs per administration.

In addition to drugs used for CM treatment, intramammary antimicrobial infusions are generally administered to all quarters of all cows at drying off. The cost for these drugs was included in the materials and investments section (see below).

Discarded Milk. On a dairy farm, milk may be discarded because of mastitis for 3 different reasons: 1) following treatment of mastitis (due to drug withdrawal time); 2) following CM cases that are not treated, but for which milk still has to be discarded until return of its normal appearance; or 3) in high SCC herds to manage bulk tank milk SCC (BMSCC) by diverting (i.e., discarding) milk of high SCC cows from the bulk tank. In the current study, these three sources of discarded milk were considered.

Milk production in Canada is regulated by a milk supply management system. In this system, milk quota cannot be leased to another farmer. Therefore, producers have to find a way to fulfil their quota despite the discarded milk. This can be achieved by increasing production of cows or by keeping more cows in order to maintain the amount of milk shipped. The last option for the farmer is to sell some quota. In the current study, we assumed that dairy producers keep more cows than needed to fill their quota to cope up with the discarded milk and milk yield reduction (assumption #2). Consequently, the extra costs associated with the discarded milk and the milk yield reduction are the costs for having the same amount of milk produced by another cow, rather than the market value of the milk (Halasa et al., 2007c).

In some situations, however, the discarded milk is used as another input on the dairy, mainly to feed calves (Vasseur et al., 2010). This practice should be discouraged due to concerns about calves' health (Wray et al., 1990, Aust et al., 2013, Brunton et al., 2014), but using the discarded milk instead of a milk replacer helps mitigate some of the losses due to the discarded milk and is still often used. However, if other readily available inputs are sufficient to feed calves (e.g., fresh cows' milk), then no additional value can be returned from the discarded milk.

In the current study, to estimate amount of discarded milk for treated CM, we took into account the proportion of CM cases in the herd that received treatment, treatment duration, drugs withdrawal time (obtained from the drug labels), and average daily milk production. Whenever a producer reported using more than one treatment regimens, mean treatment duration, mean withdrawal time, and mean treatment costs were used for CM cases occurring on this farm. Regarding non-treated CM cases, producers' reports on average time interval between CM diagnosis and time the milk from the animal has returned to the bulk tank was used instead of drug withdrawal time. Finally, amount of discarded milk for managing the BMSCC was calculated using the number of cows whose milk was discarded and duration of discarding milk for this purpose, and herd average milk production reported by producers.

For each source of discarded milk, the costs of the discarded milk could be estimated using the production cost associated with having that volume of milk produced by other cows. Whenever milk discarded following CM was used to feed the calves, the money saved on milk replacer was deducted from the discarded milk costs. In SCM, the appearance of produced milk is normal, so it may be considered healthy by producer to be fed to calves. Milk excluded from bulk tank due to high SCC was considered to be entirely used to feed calves. (assumption #3), and the money saved on milk replacer was, therefore, deducted from the discarded milk costs.

Veterinary Services. In some cases, a veterinarian is consulted regarding a, usually severe, CM case. To estimate costs for this component, the number of CM cases for which a veterinarian consultation was sought, and the average cost for a veterinary visit (excluding the drug costs) were taken into account. Dairy producers also spend money to get professional advice concerning udder health issues, which is a cost over and above treatment of a CM case (e.g. routine monitoring, outbreak investigation, high SCC problems). Amount spent on such professional advice was, therefore, also considered in the current economic model.

Labor. To estimate cost of labor associated with mastitis treatment, the average time spent working on a CM case (for diagnosis, initial treatment, follow-up treatment and separate milking), and the hourly wages were taken into account. Note that, as previously mentioned, we assumed that SCM does not result in any additional treatments during the lactation (see assumption #1); hence, no labor cost was associated with SCM treatment. However, time spent for applying various preventive measures (e.g. pre- and post-milking teat disinfection, dry cow treatment) were considered in the current study. For these later costs, we assumed one second per teat for pre- and post-milking teat disinfection, and 2 minutes per cow for administration of dry cow treatment. The required time for pre- and pos- milking disinfection and dry cow therapy was adapted from the study by van Soest et al. (2016a).

Product Quality. Additional costs associated with product quality may occur because of premium loss or penalty payment for high BMSCC. Contamination with antimicrobial residues is another factor threatening product quality. In addition to penalty paid and premium lost, cost of insurance for milk quality (e.g. to cover antimicrobial residues or high BMSCC problem) paid was also taken into account for this component. Since premium program of milk quality varies among provinces, provincial milk boards were contacted to collect information on premium program of each province (e.g., threshold for high quality milk, premium payment value), but producers were directly surveyed for information on penalty and insurance payments.

The effect of milk quality on cheese yield, shelf-life and consumers' complaints were considered to mainly influence the milk processing companies, not dairy farms (assumption #4); therefore, these costs were not included in current calculations.

Diagnostics. Producers may collect milk samples from cows having CM or SCM. To estimate cost associated with diagnostics, total number of samples collected in a year for CM and SCM, apart from regular DHI tests, and analysis cost per samples were taken into account. In addition, it was not clear whether DHI cost should be considered as mastitis-associated expenses (due to the SCC measurements). We contacted both Canadian DHI companies and producers to figure out the main motivations for participation in DHI programs. The main motivation of producers for participation in DHI programs was monitoring the nutrients of the milk (e.g., fat and protein content), the associated cost was not entitled to be included in diagnosis cost in the economic model.

Culling and Mortality. When a primiparous cow is culled or dies, costs incurred can be assumed to be those of rearing or buying an equivalent first lactation cow minus any money received for meat or milk sale. When a multiparous cow is culled or dies, the difference in milk production between the culled and replacement cow (assuming the replacement cow is a primiparous cow) was added to the cost. However, when a cow dies on farm from CM, no money is received in exchange for meat or milk sale. Furthermore, in this latter case expenditures for carcass disposal have to be considered.

Cost for primiparous cows that were culled or died were estimated using the number of first lactation cows which were culled due to CM or SCM or died due to CM, the costs for rearing or buying a replacement first lactation cow, the money received for meat or milk sale, and, for dead primiparous cows, the cost for carcass disposal.

When estimating cost for replacing a multiparous cow, these same factors were taken into account. In addition, the fact that a mature cow produces 1.3 times more milk than a first lactation was considered (Friggens et al., 1999). In the current study, we assumed that no cow died from SCM (assumption #5).

Materials and Investments. Among expenditures for mastitis prevention measures, only those performed exclusively for mastitis prevention were taken into account. These included pre- and post-milking teat disinfection, use of gloves for milking, dry cow therapy, and mastitis vaccination. Other measures such as milking machine maintenance, towels, bedding and floor management, manure collection, and other measures used for environmental hygiene were not accounted for, since these measures would still have to be used if it was not from mastitis, or are implemented to control a range of diseases such as lameness, gastrointestinal infections, etc.

Data Collection Tools

All variables needed for the economic model are listed in Table VI. The main data collection tool used to collect information on mastitis-associated expenditures in Canadian dairy herds was a questionnaire consisting of 35 open-ended and multiple-choice questions. The questionnaire was first developed in English and then translated to French (see Annex 1 and 2). The questionnaire was mailed in January 2016 to the 374 dairy producers participating in the second phase of the Canadian National Dairy Study (**CNDS**; (Belage et al., 2016)). This latter study is similar to the National Animal Health Monitoring Study (NAHMS dairy) conducted every 7 years in the United States (McConnel et al., 2015). In the CNDS, an initial general survey was sent to all Canadian registered dairy farms, and 1,193 producers completed this first survey with response rate of 11% (Belage et al., 2016). In that initial survey, participants were asked if they were willing to participate in a phase two study involving answering additional questionnaires and on farm visits. Among the initial respondents, 825 agreed to participate in the phase 2 study and a random sample of 374 dairy farms was selected for the second phase of the CNDS. The 374 farms were selected so the proportion of producers by province and of DHI-participating herds reflected the official records from the provincial dairy boards (British Columbia, n=20; Alberta, n=20; Saskatchewan, n=10; Manitoba, n=10; Ontario, n=133; Québec, n=121; New-Brunswick, n=17, Nova-Scotia, n=18; Prince Edward Island, n=20, and Newfoundland; n=5). A questionnaire was sent by mail, in the language of communication previously indicated by the dairy producer in the phase 1 of the CNDS. A 10 Canadian dollar (**CAD**) gift card incentive was provided for completing the questionnaire.

To estimate CM incidence, dairy producers were asked about the number of CM cases on their farm in the last 12 months. In the questionnaire, a CM case was defined as a cow producing abnormal milk (flakes, watery…) with or without a swollen udder, fever or loss of appetite. Subclinical mastitis was also referred to as “elevated SCC”. In the general section of the questionnaire, questions on the number of milking cows, average production per cow per day, and mean BMSCC were included. The questionnaire is available upon request.

The costs of the intramammary treatments reported to be used were based on retail prices suggested by the largest Canadian veterinary drug distributor (CDMV, St-Hyacinthe, QC). For producers who reported using more than 1 type of intramammary drugs to treat CM, we used the mean price of the various treatments reported to be used.

In our economic model, severe CM cases were deemed to receive systemic treatment in addition to intramammary treatment. To determine proportion of CM cases being severe, the database of the Canadian Bovine Mastitis and Milk Quality Research Network's National Cohort of Dairy Farms was consulted (Reyher et al., 2011). In short, in this cohort the cows from 91 farms were followed in 2007 and 2008, and all CM events as well as severity of these events were recorded on a 1 to 3 scale as described by Sears et al. (2003b). In this study, a severity score of 3 (i.e. severe CM) was observed in 20% of CM cases when using the 74 herds validated for CM reporting (Elghafghuf et al., 2014). We therefore assumed that 20% of the CM cases reported by dairy producers would be severe cases and treated with both local and systemic treatments. In severe cases, additional costs due to systemic antimicrobial (3 doses of 9.6 g of trimethoprim/sulfamethoxazole) and anti-inflammatory (1 single dose of 1.3 g of flunixin meglumine) injections were estimated at 25.40 CAD using, again, retail prices suggested by CDMV.

Costs for production of 1 kg of milk was obtained from the Cost of Production Study (2016a) conducted by the Canadian Dairy Commission. Using this later study conducted on a sample of 234 dairy farms, cost of production was established at 0.78 CAD/kg of milk. Regarding costs of milk replacer, the retail prices of the 5 most popular brands of milk replacer were obtained through internet resources and phone calls to distributors. Taking into consideration the mixing directions for each brand, a mean price of 0.49 CAD/litre (range: 0.42, 0.62 CAD) of reconstituted milk replacer was obtained and used as a fixed value.

Finally, based on labor wages used in the Cost of Production Study and obtained from Statistics Canada (Canadian Dairy Commission, 2016a), wages for dairy personnel (most often the owner and its family on Canadian dairy farms) were fixed at 34.50 CAD/hour (Statistics Canada, 2015).

Data Management and Statistical Analyses

All returned questionnaires were coded and entered in a database (Access 2016, Microsoft Corp., Redmond, WA). Specific codes for missing, not applicable, and unreadable responses were used. The database was then transferred to SAS 9.4 (SAS Institute Inc., Cary, NC) for computation of indices and descriptive statistics. For each quantitative variable, minimum, standard deviation, first quartile, mean, median, third quartile, and maximum were calculated. Unlikely values were identified and impossible responses were excluded from calculation. The distribution of each variable was depicted to evaluate the normality of the distribution.

Then, for each herd, expenses due to the different mastitis-related components were computed by applying the values reported by the dairy producer to the equations reported in Appendix A. On a few occasions one of the producer's answer was incomplete and precluded computation of expenses, in these cases the median observed value was used instead. For instance, a few producers reported having culled cows due to mastitis, but did not report the price received for culled cows. For these the median price for culled cows observed in the dataset was used.

Expenses that could be attributed to either CM or SCM were summed separately. All expenses were then multiplied by 100 and divided by the number of milking cows to report cost/100 milking cows. Clinical mastitis-related expenses were also reported as CAD/CM case by dividing total amount spent for CM-related expenses by number of CM cases reported.

For each herd, proportion of the cost attributable to a specific component was also computed by dividing absolute cost for this component by total herd mastitis-related expenditures. Proportion of the mastitis-related expenses due to CM, SCM, and other expenditures were computed in a similar manner.

2.4 RESULTS

Between January and May 2016, 145 producers responded to the questionnaire (39% response rate). Median number of milking cows was 60 (range: 20 to 550 cows) with an average milk production of 32 kg/day (SD: 5.7 kg). Median self-reported incidence of CM was 19 cases/100 cow-years (Q1 and Q3 of 11 and 31 cases/100 cow-years, respectively; Figure 6). Mean self-reported BMSCC was 184,000 cells/mL (SD: 69,000 cells/mL; Figure 7), and 67% of respondents participated in DHI.

Adoption of various mastitis-preventive measures is presented in Table VII. Most producers reported using post-milking teat disinfection (97%) and dry cow therapy (93%), and a substantial proportion of producers reported using pre-milking teat disinfection (79%) and wearing gloves during milking (77%). Using vaccination for preventing mastitis was used by a minority of producers (35%). Distribution of mastitis costs attributable to CM, SCM, materials and investment, and product quality are presented in Table VIII and are discussed for each costs component in the following sections.

Milk yield reduction

Median economic value of milk yield reduction following CM cases was estimated at 6,703 CAD/100 cows-year (range: 0 to 41,632). Median economic value of milk yield reduction due to SCM was estimated at 24,110 CAD/100 cows-year (range:0 to 47,057).

Drugs

Ten (7%) producers indicated that their farms were certified organic. Median proportion of CM cases that were treated in all herds including both organic and commercial was 90%. Most producers used intramammary infusion solely, with treatment duration ranging from 1 to 9 d. Median cost for treatment of mild or moderate CM was 21 CAD and median cost for drugs for severe CM was 46 CAD. Total drug expenditure for treatment of CM was estimated at 349 CAD/100 cows-year (range: 0 to 5,908).

One interesting finding regarding drugs used for CM treatment is that producers often treated cows for longer duration than the labelled treatment regimen. Seventy producers reported one single treatment protocol used for their typical mild or moderate CM case, so their treatment protocols could be compared to the labelled drug regimen. Among these producers, only 12 (17%) reported using the labelled treatment protocol. Among the 58 (83%) producers using off-label treatments, 2 (4%) treated for 1.5 d with a product labelled for a 2-d treatment, and 54 (93%) treated for longer than the label recommended (mean: +2 d; range: 0.5 to 6 d). A total of 14 (24%) producers used the drugs with higher administration frequency (i.e. twice a day administration of a product labelled for once a day administration), and 3 (5%) producers reported using drugs with a lower administration frequency (i.e. once a day administration of a product labelled to be administered twice a day).

Discarded Milk

The median period milk was discarded in case of CM treatment was 6 d (range: 4 to 12 d), which included treatment days plus drug withdrawal time; whereas, in cows with untreated CM the median duration of discarding milk was 2 d (range: 0-21 d). Most producers reported using a substantial proportion of milk discarded due to CM to feed calves (median: 25% of discarded milk; range: 0 to 100%). Median cost of discarded milk due to both treated and untreated CM after subtracting the value of wasted milk fed to calves was 1,445 CAD/100 cow-year (range: 0 to 12,007), and median cost of discarded milk for one CM case was 79 CAD/CM case (range: 2 to 686).

Among participating producers, 41% reported discarding milk of cows with high SCC. Overall median number of cows per year for which milk was discarded was 1 cow per year (range: 0 to 37) and the milk of these cows was discarded on average during 7 days (range: 0 to 100). Amount of discarded milk due to SCM was not significantly associated with the BMSCC (i.e., low and high SCC herds equally discarded milk due to SCM). Median costs of discarded milk for high SCC cows were estimated at 87 CAD/100 cow-year (range: 0 to 10,150 CAD).

Veterinary Services

Producers reported calling a veterinarian for less than 1% of CM cases (range: 0 to 75% of CM cases) and median cost for a veterinary visit (excluding drugs) was 100 CAD. Consequently, median veterinary cost for CM cases were 0 CAD/100 cow-year (range: 0 to 3,396 CAD).

In addition, only 24% of producers reported having used a veterinarian for udder health monitoring, high SCC, or CM outbreak investigation in the last 12 months. Median costs for veterinary services for such monitoring or investigation was, therefore, estimated at 0 CAD/100 cows-year (range: 0 to 9,375).

Labor

Median time working on a CM case (for diagnosis, initial treatment, follow-up treatments and separate milking) was 1 h (range: 0 to 8.5 h). Median expenditures for extra labor due to CM was estimated at 657 CAD/100 cow-years (range: 0 to 9,554), and 34 CAD/CM case (range: 3 to 239).

Product Quality

Having to pay a penalty for high BMSCC milk is relatively uncommon in Canada. Nevertheless, among our respondents, 3 producers reported paying penalties (one of 100 CAD, one of 500 CAD, and the last one 5,000 CAD) within 12 months. Median costs for penalty were, therefore, estimated at 0 CAD/100 cow-year (range: 0 to 3,759 CAD). Proportion of respondents who had insurance coverage for antimicrobial residues in milk was 66%; however, many respondents did not know the exact portion of their insurance payment being specifically for milk quality insurance. The median annual costs for insurance was 0 CAD/100 cow-year (range: 0 to 2,857).

Milk quality premium system varied among provinces. In some provinces (Ontario, Newfoundland and Labrador, Nova Scotia), producers did not receive bonus for milk quality, so premium loss was considered zero for herds located in these provinces. In New Brunswick, there was no per hectoliter premium system. Instead, the offered premium on milk quality was a yearly cash awards to the 10 producers who had the best milk quality results. Therefore, premium loss was not considered for herds in New Brunswick.

In the Western provinces (Alberta, British Columbia, Manitoba, Saskatchewan), a premium was paid to herds with average BMSCC ≤ 250,000 cells/mL, whereas, in Quebec and Prince Edward Island the threshold was BMSCC ≤ 200,000 cells/mL. Mean value of premium in western provinces, Quebec, and Prince Edward Island was 0.28, 0.50, and 0.25 CAD/hl respectively. Moreover, in Quebec there was an additional 0.29 CAD/hl premium for herds with BMSCC ≤ 150,000 cells/mL.

Because many herds were located in provinces were no milk quality premiums were distributed, and because many of the herds in provinces having milk quality premiums did get that premiums, losing a premium for milk quality was an uncommon event (n=37 herds). Median estimated value for premium loss was 0 CAD/100 cows-year (range: 0 to 11,534).

Diagnosis

The proportion of herds reporting collecting and analyzing (sent to the laboratory or analyzed on farm) milk samples from CM cows was 66%. Median expenditures for diagnosis of CM were 59 CAD/100 cow-year (range: 0 to 3,378 CAD). Fifty percent of producers reported submitting milk samples from cows suspected of SCM for bacteriological culture, and median costs of 0 CAD/100 cow-year (range: 0 to 7,500 CAD) were observed for SCM diagnosis.

Based on producers' responses, main motivation of most producers (82%) for participation in DHI program was not monitoring cows' SCC, and most reported that they would still pay for DHI participation even without any SCC information. Therefore, although 68% of herds were participating in DHI programs with a median frequency of 10 herd tests per year, membership fees for DHI programs were not considered as a mastitis-associated expenditure and were excluded from our calculations.

Culling and Mortality

Among respondents, 54% and 17% reported having culled or lost, respectively, first lactation cows due to CM in the last 12 months. Median number of culled and dead heifers due to CM were respectively of 0 (range: 0 to 23) and 0 animal/100 cow-year (range: 0 to 12). Median cost for 1 culled heifer was 1,350 CAD. Median cost for culled heifers was 0 CAD/100 cow-year (range: 0 to 46,154 CAD). Median costs attributable to heifers dying from CM were 0 CAD/100 cow-year (range: 0 to 31,800 CAD).

A total of 86% and 39% of respondents, respectively, reported having culled or lost ≥ 2nd lactation cows due to CM in the last 12 months. Median number of culled and dead cows due to CM were 3 (range: 0 to 21) and 0 animals/100 cow-years (range: 0 to 9), respectively. Median cost for culling 1 cow was 2,150 CAD/culled cow. Median costs attributable to culling ≥ 2nd lactation cows were 5,911 CAD/100 cow-year (range: 0 to 58, 585 CAD). Median costs for ≥ 2nd lactation cows dying from CM were 0 CAD/100 cow-year (range: 0 to 33,913 CAD). Consequently, median costs associated with culling and mortality of heifers and mature cows were 9,037 CAD/100 cow-year (range: 0 to 61,304 CAD).

A total of 47% and 84% of dairy producers reported having culled heifers and cows, respectively, due to SCM in the last 12 months. Median number of heifers culled for SCM was 0 animals/100 cow-year (range: 0 to 23 animals). Median number of cows culled for SCM was 4 animals/100 cow-year (range: 0 to 22 animals). Median costs for culling heifers due to SCM in a 100-cows herd was 0 CAD (range: 0 to 46,154 CAD). Median costs for culling adult cows due to SCM in a 100 cows herd was 6,743 CAD (range: 0 to 58,585CAD). Median total costs due to culling of heifers and cows due to SCM was 8,571 CAD (range: 0 to 58,585 CAD).

Material and Investment

Median costs of prevention measures are indicated in Table VII. In terms of materials and labor, the 3 most expensive preventive measures were pre- and post-milking teat disinfection and dry cow therapy.

Relative Costs

Median expenses for a CM case were 744 CAD/CM case. Median estimated costs were 13,487 CAD/100 cow-year for CM, and 34,344/100 cow-year for SCM. Relative importance of the different cost-components for the median herd is presented in Figure 8. Overall, SCM (48%) was the costliest category, followed by CM (34%), and materials and investment (mainly for applying preventive measures; 15%). In the median herd, most of CM costs were due to culling and mortality (48%) and then milk yield reduction (34%; Figure 8). Regarding SCM, most of the costs (72%) were due to milk yield reduction and 25% were due to culling (Figure 8).

2.5 DISCUSSION

The objective of this study was restricted to describe the current cost of mastitis on Canadian dairy farms and the distribution among the different cost components. The aim of this study was to give a broad picture of these costs and, therefore, some components with a lower relative importance were not included in our calculations. For example, the potential negative effects of mastitis on cows' reproductive performances or risk of other diseases were excluded from our calculation due to uncertainty about association between mastitis and these events, not mentioning the complexity inherent to estimating these impacts. Moreover, preventive measures implemented to control both mastitis and other diseases were excluded from mastitis cost.

The estimated median CM incidence in the current study (i.e. 19 cases/100 cows-year) was close to previous estimates in Canadian dairies. In the study by Olde Riekerink et al. (2008), mean incidence rate of CM was estimated at 23 cases/100 cows-year during 2003 to 2005. In the National Cohort of Dairy Farms (**NCDF**) study, conducted in 2007 and 2008 a median incidence rate of 21.3 case/cow-305 days was reported (Elghafghuf et al., 2014). At first sight CM incidence rate may seem to be decreasing over time, but in Elghagguf et al. (2014) only the first mastitis episode was included, whereas in Olde Riekerink et al. (2008) and the current study, both first and repeated episodes were included. In addition, Elghafghuf et al. (2014) study was prospective with frequent follow-ups and more precise measurements, while in the current study, number of CM cases within 12 months reported by producers were used to estimate the overall CM incidence, which may possibly result in an underestimation. Similarly, the mean self-reported BMSCC in the current study (184,000 cells/mL) was close to reports by prior studies in Canada such as the study by Olde Riekerink et al. (2010) which reported that geometric mean BMSCC was 185,000 cells/mL.

Comparing the adoption level of preventive practices in the study of Gill et al. (1990) with the results in current study shows that among those measures that were recommended in both years 1990 and 2015, the highest increase was evident in implementing dry cow therapy which has increased by 18%. Comparing adoption levels of preventive practices in the current study and those in the study by Olde Riekerink et al. (2010) showed that practices less implemented in 2010 such as pre-milking teat disinfection, dry cow therapy, wearing gloves at milking, and using mastitis vaccines are more and more adopted by producers.

In the current study, mastitis costs appear to be substantial (662 CAD/cow-year for a typical Canadian dairy), with most of the costs (48%) being attributed to SCM (due mainly to costs attributable to the subsequent reduced milk yield), and 34 and 15% due to CM and implementation of preventive measures, respectively. Since there are no other recent equivalent studies on mastitis costs in Canada, or in other countries with a similar production system, it is difficult to directly compare these results to other studies. Nevertheless, in a study conducted in The Netherlands by van Soest et al. (2016a), preventive measures were the most expensive cost component, estimated at € 120/cow-year and representing 50% of total mastitis costs. In that same study, the next most important component was milk yield reduction (€ 69/cow-year; 29% of costs), followed by culling (€ 20/cow-year; 8%) and discarded milk (€ 20/cow-year; also 8% of costs). In the current study, the estimated costs of milk yield reduction (313 CAD/cow-year) and culling were higher (192 CAD/cow-year) than costs of preventive measures (105 CAD/cow-year) and discarded milk (19 CAD/cow-year). In addition, costs of culling and discarded milk were not presented separately for CM and SCM in van Soest et al. (2016a). Preventive measures can hardly be separated between CM and SCM since many of these measures are targeting both forms of the disease. Nonetheless, by dividing culling and discarded milk costs between CM and SCM, we were able to demonstrate, in the current study, that CM and SCM contribute almost equally to culling cost. Additionally, although discarding milk for SCM is a relatively common practice applied by Canadian dairy producers, the amount of milk discarded for this reason is small compared to that of CM.

Clinical Mastitis Cost

Regarding CM cost in the current study, highest relative cost were due to culling and mortality (48%), milk yield reduction (34%), discarded milk (11%), and, finally, labor (3%). In a Dutch study conducted when The Netherlands still had a supply management system for dairy (Huips et al., 2008), milk yield reduction and culling were identified as the two most substantial CM cost components with a mean cost of € 23/cow-year and € 22/cow-year, respectively. These two components were followed by cost of discarded milk (€ 9/cow-year) and then drugs (€ 6/cow-year). However, the three components of CM costs with highest values in the current study were in order culling, milk yield reduction, and discarded milk. Differences in relative importance of CM cost components in these two studies could be due to considerable differences in inputs such as cost of culling per cow and frequency of culling in CM cases. Moreover, in the current study additional cost of replacing culled multiparous cows by heifers due to their differences in milk production was taken into account. In contrast, in Huijps et al. (2008b) a fixed value (€ 480) was used as costs of culling a cow regardless of the cow parity. In a Finnish study, also conducted when there was a milk supply management system, milk yield reduction (31%), veterinary services and drugs (24%), premature culling (23%), and then discarded milk (18%) had highest shares in total CM costs (Heikkila et al., 2012). A noticeable difference between our study and that of Heikkila et al. (2012), is that in Finland, unlike Canada, only veterinarians are authorised to treat mastitis cases. Therefore, CM treatment was much more expensive in Finland than in Canada, where veterinarians are called for less than 1% of CM cases.

Subclinical Mastitis Cost

The only cost component for SCM that was measured specifically in the aforementioned studies was reduced milk production (Huijps et al., 2008b, van Soest et al., 2016a). To our knowledge, other components such as culling and discarded milk were never presented separately for CM and SCM. It is, therefore, difficult to compare our results with those of previously published studies. In the current study, the two most substantial cost components of SCM were milk yield reduction (72%) and culling (25%). Although costs of veterinary advices for SCM control were reported to be near zero (Figure 8), these costs are possibly underestimated by dairy producers since these veterinary consultations are often intertwined with other activities (e.g. reproduction, calve health) occurring during regular herd health visits.

Preventive Measures Cost

Van Soest et al. (2016) estimated cost of preventive mastitis control measures on Dutch dairy farms at € 120/cow-year, which was higher than costs of other important components such as milk yield reduction and culling. The main contributor to preventive cost was the required labor to implement practices. It is noteworthy, however, that preventive measures considered by van Soest et al. (2016) were less mastitis-specific and included practices that are not performed exclusively for mastitis control (e.g., cleaning alley ways, cleaning cubicles). Whereas, by considering practices used exclusively for mastitis (i.e. pre- and post-milking teat disinfection, dry cow treatment, wearing gloves during milking, and mastitis vaccines), as in the current study, application of preventive measures was, of course, less expensive (105 CAD/cow-year).

Potential Biases

Some factors in the current study may have led to an underestimation of mastitis costs. For estimating CM costs, a single milk production ratio (1.3:1.0) between multiparous and primiparous cows was considered in our computations, whereas this ratio is for comparing second and first lactation cows. The milk production ratio of third to first lactation cows would actually be slightly higher (Friggens et al., 1999). Furthermore, older cows (i.e. ≥ 3 lactations) have higher risk to die or to be culled following CM (Thomsen et al., 2004, Pinedo et al., 2010). Therefore, a considerable proportion of mature cows that died or were culled because of mastitis were possibly cows with ≥ 3 lactations. Consequently, CM culling costs were possibly underestimated. In addition, most CM cases occur in early lactation (de Haas et al., 2002) which is the time when the cow is producing the most. This fact was not taken into account in the current study, since mean milk production was used to compute amount of discarded milk, resulting, again, in an underestimation of CM discarded milk costs.

In the current study, we also considered that SCM cases were not treated during the lactation, while, actually, some producers certainly used this practice. Such an assumption possibly led to an underestimation of drugs costs and of milk discarded due to SCM. Nevertheless, treating cows during the lactation for SCM would not be very common in Canada and the impact of that later assumption is likely to be small.

Feeding calves with raw waste milk have negative impacts on calf and herd health by increasing the risk of antimicrobial resistance and bacterial shedding in the environment (Wray et al., 1990, Aust et al., 2013, Brunton et al., 2014). However, in the current study the negative economic consequences of this practice were not taken into account.

Number of cows culled due to CM or SCM, a very important component of mastitis cost, was reported by dairy producers using retrospective data. Culling decisions, however, are mostly taken based on more than one single reason (Fetrow et al., 2006). Therefore, depending on the producers' considerations when answering that specific question, proportion of mastitis-culled cows may have been over- or underestimated. In this case, direction of bias is difficult to predict. However, we could hypothesize that dairy producers would more likely forget to complete some of their records regarding culling, than complete extra records. Therefore, the number of cows reported to be culled because of mastitis is likely to be an underestimation, which may, in turn, compensate for the fact that, for some of these cows, mastitis was possibly a minor component in the culling decision (e.g. a 305 DIM, low producing, open cow with mastitis would likely eventually be culled without the mastitis event).

Premium losses were determined based on mean BMSCC reported by producers solely. However, there were other criteria for milk quality to get entitled for premium payment (e.g., individual bacterial count) which were not available to the authors. Moreover, annual mean BMSCC was used for this purpose instead of monthly mean; consequently, the estimated value of premium loss could be biased. Since median relative costs of product quality were estimated 0%, the mentioned biases had no considerable impact on overall costs.

The figures obtained in the current study will be used to develop an economic model to be applied to all Canadian dairy farms using retrospective demographic data available in DHI and previous mastitis knowledge obtained from the National Cohort of Dairy Farms (Reyher et al., 2011) to compute mastitis cost in Canada and to monitor mastitis cost fluctuations over time.

2.6 CONCLUSION

Cost of mastitis in Canadian dairy herds was substantial with median costs of 662 CAD/cow-year. Among the different components, milk yield reduction was the highest costly component (313 CAD/cow-year; 46%). Cost for culling and implementation of preventive measures were the second and third most important cost components, respectively.

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Table VI. Variables used to estimate costs for mastitis-related expenditures, culling, and discarded milk.

Component	Required variables
General information	Number of milking cows
Milk yield reduction	Mean BMSCC, number of milking cows, costs of production of 1 kg of milk [a], Number of CM cases, cow mean daily milk production
Drug	Number of CM cases, proportion of CM cases that were severe[b], proportion of moderate and mild CM cases that received treatments, type of drugs used, frequency of administration and duration of treatment, price per drug unit[c]
Discarded milk	Number of CM cases, proportion of CM cases that received treatment, average duration of treatment, withdrawal time of used drugs[d], duration of discarding milk in CM cases that are not treated, number of cow-days of discarding milk to manage BMSCC, mean cow daily milk production, costs of production of 1 kg of milk[a], proportion of discarded milk fed to calves, price milk replacer[e]
Veterinary services	Number of CM cases, proportion of CM cases visited by a veterinarian, average cost for a veterinary visit, expenses on professional advices regarding herd mastitis issues
Labor	Number of CM cases, average time spent working on a CM case, average hourly wage[f]
Product quality	Cost of insurance, amount paid in penalties, premium loss

Diagnostic	Number of samples collected in a year for CM and SCM apart from regular DHI tests, costs per sample
Culling/mortality	Number of first lactation and older cows which were culled or died due to CM or SCM, costs for rearing or buying a first lactation cow, difference in milk production between primiparous and multiparous[g], money received for meat or milk when selling a cow, money spent on carcass disposal for dead cows
Materials and investments (Material and labor for implementing preventive measures)	Expenses for pre- and post-milking teat disinfection, gloves used for milking, dry cow therapy, and mastitis vaccination, required labor time for implementing pre- and post-milking teat disinfection and dry cow therapy[h]

All values were reported for last 12 months (i.e., year 2015). Unless specified otherwise, source of information for variables was the producers' questionnaire sent to the 374 Canadian National Dairy Study participants.

[a] Source: Canadian Dairy Commission 2015 cost of production study http://www.cdc-ccl.gc.ca/CDC/userfiles/file/REPORT_-_P&E_-_2015_COP_Indexed_to_Q1_2016_Booklet_-_July_2016.pdf.

[b] Source: Canadian Bovine Mastitis Research Network National Cohort of Dairy Farm study (Reyher et al., 2011)

[c] Source: suggested retail price of the largest Canadian veterinary drug distributor (CDMV) St-Hyacinthe, QC, Canada, https://www.cdmv.com/en/veterinary-boutique.sn

[d] Source: drug labels

[e] Source: mean retail price of the 5 most popular brands

[f] Source: Statistics Canada http://www5.statcan.gc.ca/cansim

[g] Friggens et al., 1999

[h] van Soest et al., 2016

Table VII. Adoption proportion of various mastitis-preventive measures in 2015 in a sample of 145 Canadian dairy producers.

Prevention measure	Adoption proportion (%)	95% Confidence interval (%)
Pre-milking teat disinfection	79	73 - 83
Post-milking teat disinfection	97	94 - 99
Dry cow therapy	93	89 - 97
Wearing gloves at milking	77	70 - 84
Use of mastitis vaccines	35	27 - 43

Table VIII. Herd distribution of mastitis-related costs (in CAD/100 cows/year) in 2015 in a sample of 145 Canadian dairy producers.

Component	Min	Percentiles			Max	Mean	SD
		25th	50th	75th			
Clinical Mastitis							
Milk yield reduction	0	4,213	6,703	10,773	41,632	8,522	7,026
Drugs	0	131	349	694	5,908	511	644
Discarded milk	0	817	1,445	2,580	12,007	2,104	1,984
Veterinary services	0	0	0	161	3,396	155	393
Labor	0	310	657	1,294	9,554	1,194	1,676
Diagnosis	0	0	59	226	3,378	187	381
Culling and mortality	0	4,605	9,037	17,222	61,304	14,045	14,045
Total clinical mastitis	0	13,372	19,889	33,439	94, 253	27, 631	19,981
Subclinical mastitis							
Milk yield reduction	0	17,928	24,110	32,217	47,057	24,461	10,041
Discarded milk	0	0	87	548	10,150	532	1,280
Veterinary services	0	0	0	0	9,375	266	1,112
Diagnosis	0	0	0	217	7,500	230	732
Culling	0	3,229	8,571	15,600	58,585	11,653	12,401
Total subclinical mastitis	2,345	24,162	34,859	46,405	98,381	37,048	18,027
Materials and investments (Prevention measures)							
Materials pre-milking teat disinfection	0	200	969	1,585	7,619	1,193	1,251
Labor pre-milking teat disinfection	0	2,758	2,758	2,758	2,758	2,187	1,121
Materials post-milking	0	920	1,500	2,610	6,714	1,937	1,452

teat disinfection							
Labor post-milking teat disinfection	0	2,758	2,758	2,758	2,758	2,606	632
Materials dry cow therapy	0	943	1,683	2,500	16,667	1,837	1,740
Labor dry cow therapy	0	91	91	91	91	81	28
Gloves	0	23	156	386	1,800	251	283
Vaccines	0	0	0	571	4,650	422	836
Total Prevention measures	0	8,106	10,477	13,134	24,495	10,515	4,236
Product quality							
Insurance	0	0	0	105	2,857	133	381
Penalty	0	0	0	0	3,759	35	325
Premium loss	0	0	0	1,164	11,534	1,394	2,791
Total product quality	0	0	0	2,843	11,912	1,564	2,828
Total	16,508	51,014	66,178	93,634	182,581	76,657	35,400

Min: minimum; Max: maximum

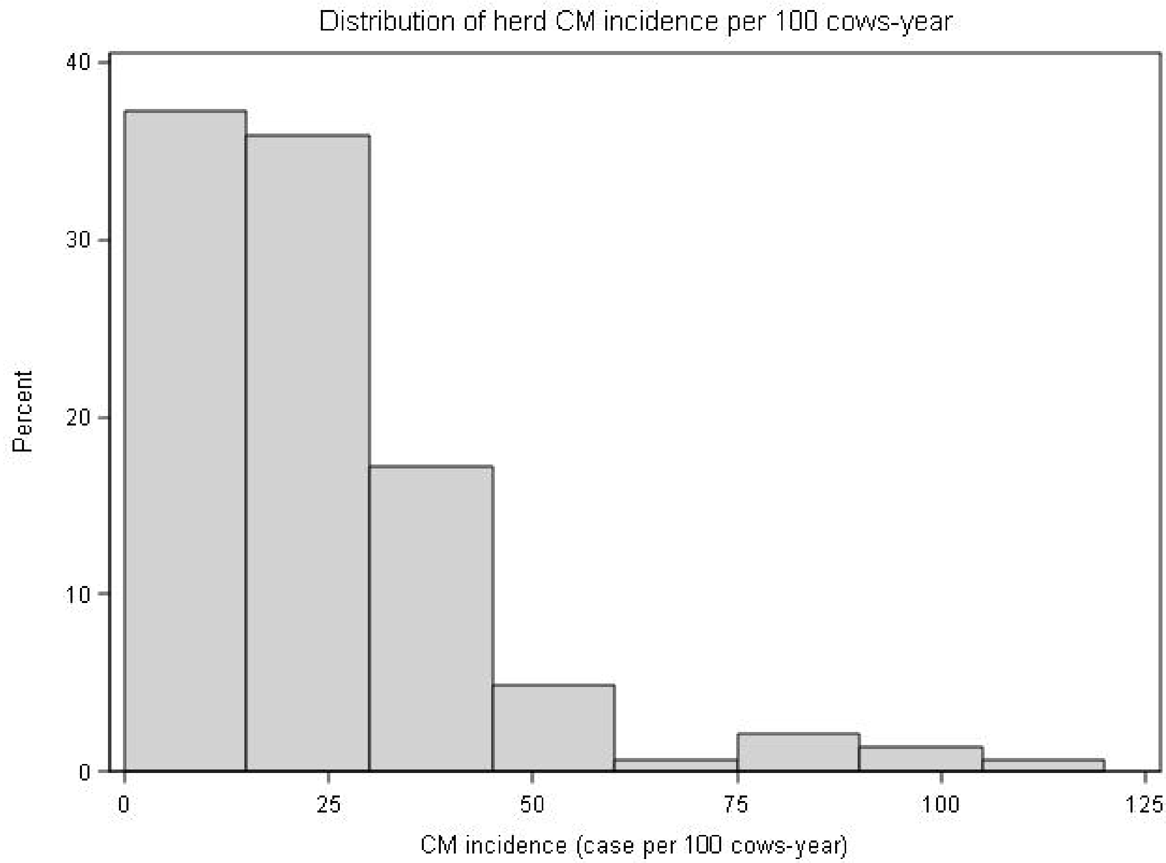

Figure 6. Distribution of clinical mastitis incidence (in CM cases/100 cow-years) in 2015 based on producers' reports in a sample of 145 Canadian dairy producers.

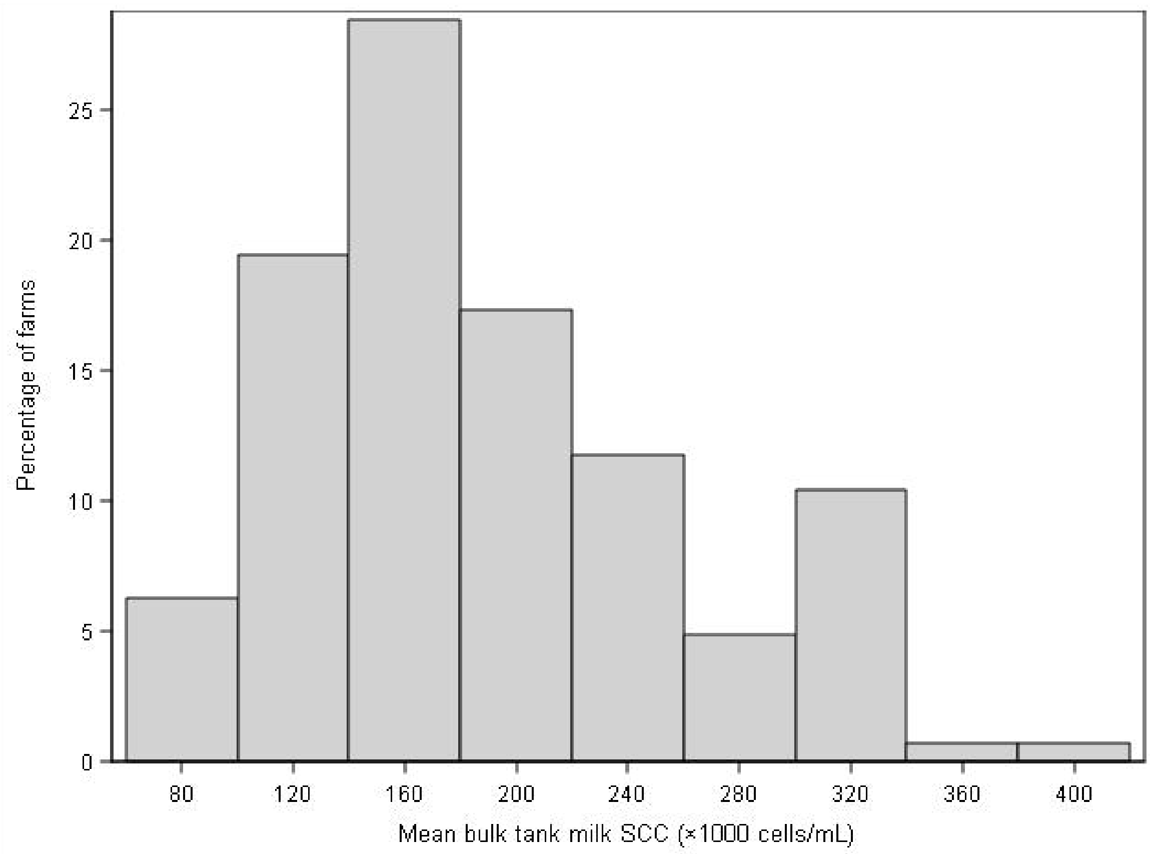

Figure 7. Distribution of mean 2015 bulk milk SCC in a sample of 145 Canadian dairy producers.

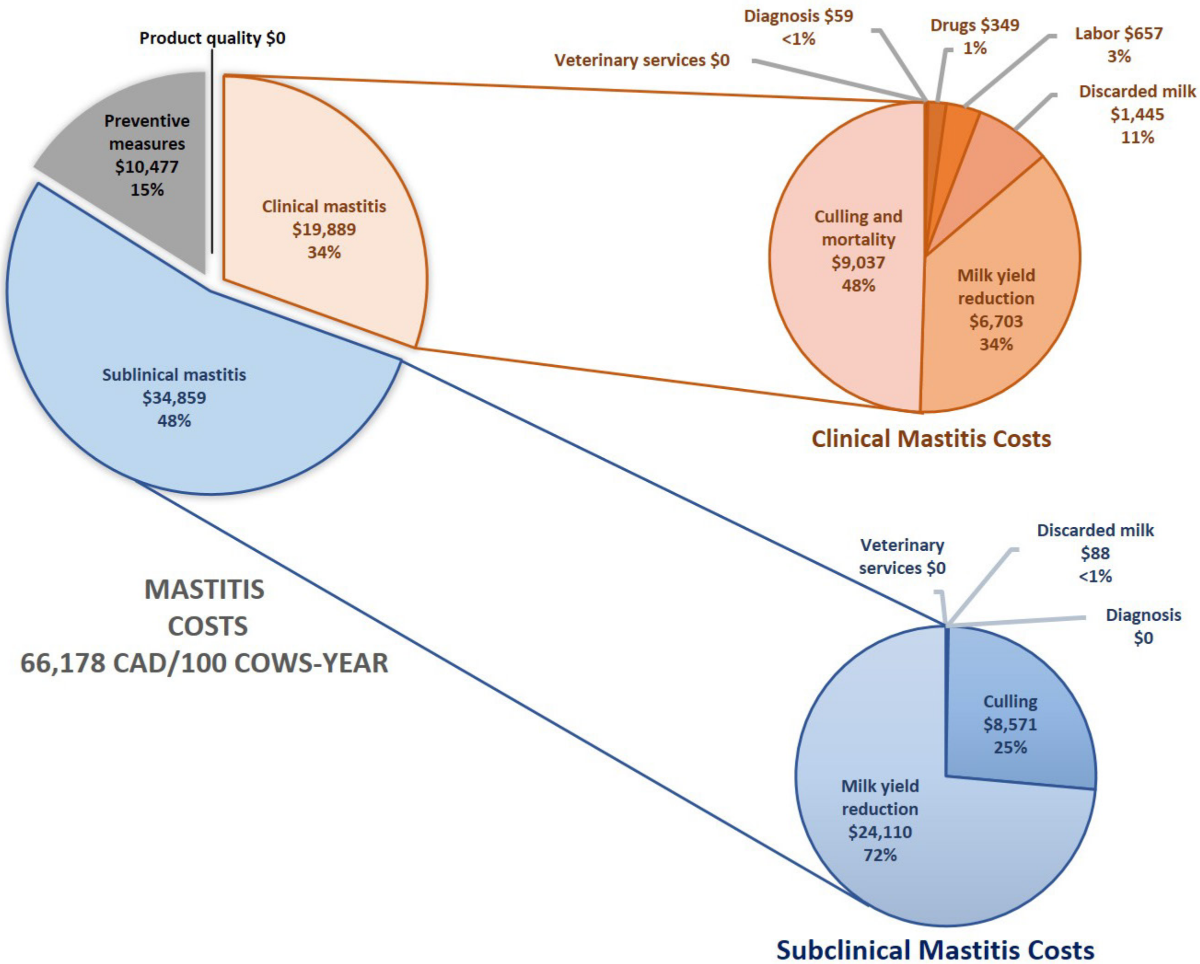

Figure 8. Absolute values and relative importance (in %) of the different cost-components for the median herd in Canada (100 cows-year)

2.9. APPENDIX A

Component	Equation	
Milk yield reduction	Eq. 1	Amount of herd milk loss due to CM = number of CM cases × 0.05[a] × mean cow daily milk production × 305[b]
	Eq. 2	Costs of milk loss due to CM = amount of herd milk loss due to CM × 0.78[c]
	Eq. 3	Average linear score of individual cow SCC in herd = (Log10(BMSCC) -1.6)/0.24[d]
	Eq. 4	Amount of milk loss due to SCM=number of milking cows×190[d]× (Average linear score of individual cow SCC in herd -1)
	Eq. 5	Costs of milk loss due to SCM = Amount of milk loss due to SCM×0.78[c]
Drug	Eq. 6	Cost of drugs for total local treatment= mean price of used intramammary infusions per quarter per day × days of treatment × frequency of treatments per day
	Eq. 7	Cost of drugs to treat mild to moderate CM = number of CM cases × 0.8[e] × proportion of CM cases receiving treatment × cost of drugs for total local treatment
	Eq. 8	Cost of drugs to treat severe CM = number of CM cases × 0.2[e] × proportion of CM cases receiving treatment × (cost of drugs for total local treatment + 25.4[f])
	Eq. 9	Total cost of CM treatment= Cost of drugs to treat mild to moderate CM + Cost of drugs to treat severe CM
Discarded milk	Eq. 10	Amount of milk discarded for treated CM = number of CM cases × Proportion of CM cases treated × (duration of treatment + mean withdrawal time) × average daily milk production per cow
	Eq. 11	Amount of milk discarded for untreated CM = Number of CM cases × (1- Proportion of CM cases treated) × number of days before milk is put back in bulk tank × average daily milk production per cow
	Eq. 12	Total amount of milk discarded in CM cases (treated + untreated) = Amount of milk discarded for treated CM + Amount of milk discarded for untreated CM
	Eq. 13	Economic impact of discarding milk in CM cases = (total amount of milk discarded in CM cases × 0.78[c]) – (% of discarded milk used to feed calves × total amount of milk discarded in CM × 0.49[g])
	Eq. 14	Amount of milk discarded for SCM = Number of cows excluded from bulk tank for high SCC × number of days of this exclusion × mean daily milk production per cow
	Eq.15	Economic value of discarding milk in SCM cases = (Amount of milk discarded for SCM × 0.78[c]) – (Amount of milk discarded for SCM ×0.49[g])

Component	Equation	
Veterinary services	Eq.16	Cost of veterinary services for CM = number of CM cases × proportion of CM cases for which veterinarian is called × average cost for a veterinary visit
	Eq.17	Cost of veterinary services for herd SCC management = total expenditures on professional advices about herd mastitis issue
Labor	Eq.18	Cost of labor to manage CM = number of CM cases × time spent working on a CM case (diagnostic, initial treatment, follow-up treatment, separate milking) ×34.5[i]
Product quality	Eq.19	Cost of milk quality = yearly payment for insurance in case there is an insurance coverage + penalty payment for exceeding SCC limit + premium loss for exceeding SCC limit
Diagnostic	Eq.20	Cost of diagnostic procedure for CM = number of samples collected in a year for CM × cost of each sample
	Eq.21	Cost of diagnostic procedure for SCM = number of samples collected in a year for SCM cases × cost of each sample
Culling and mortality	Eq.22	Economic value of culling of 1st lactation cows for CM = Number of 1st lactation cows culled due to CM × (costs for rearing or buying a 1st lactation cow - money received for meat or milk sale)
	Eq.23	Economic value of 1st lactation cows dying from CM = Number of 1st lactation cows that died due to CM × (costs for rearing or buying a 1st lactation cow + money spent for carcass disposal)
	Eq.24	Economic value of culling of older cows for CM = Number of older cows culled due to CM × (1.3[h] × costs for rearing or buying a 1st lactation cow - money received for meat or milk sale)
	Eq.25	Economic value of older cows dying from CM = Number of older cows that died due to CM × (1.3[h] × costs for rearing or buying a 1st lactation cow + money spent for carcass disposal)
	Eq.26	Economic value of culling 1st lactation cows due to SCM = Number of 1st lactation cows culled due to SCM × (costs for rearing or buying a 1st lactation cow - money received for meat or milk sale)
	Eq.27	Economic value of culling older cows due to SCM = Number of older cows culled due to SCM × (1.3[h] × costs for rearing or buying a 1st lactation cow - money received for meat or milk sale)
Materials and investments (with required labor)	Eq.28	Economic value of required labor for pre-milking teat disinfection in 12 months= number of milking cows× (4/3600) [j] × 2[k] ×365[l]× 34.5[i]
	Eq.29	Economic value of required labor for post-milking teat disinfection in 12 months= number of milking cows× (4/3600) [j] × 2[k] ×365[l]× 34.5[i]
	Eq.30	Economic value of required labor for dry cow therapy in 12 months= number of milking cows×0.8[m] × (2/60) [n]× 34.5[i]
	Eq.31	Cost of pre-milking teat disinfection in 12 months + Economic value of required labor for pre-milking teat disinfection + Cost of post-milking teat disinfection in 12 months + Economic value of required labor for post-milking teat disinfection + Cost of dry cow therapy in 12 months + Economic value of required labor for dry cow therapy

Component	Equation	
		+ Cost of gloves used during milking in 12 months + Cost of mastitis vaccine in 12 months

All costs were multiplied by 100 and divided by number of milking cows to report value for a herd of 100 milking cows. Values were mostly obtained from producers through questionnaires except for factors with superscripts explained in following footnotes:

[a] (Seegers et al., 2003b)

[b] Days in 1 lactation

[c] Cost of producing 1 litre of milk in 2015 in Canadian dollar (Canadian Dairy Commission, 2016a)

[d] (Fetrow et al., 1988)

[e] Proportion of mild to moderate versus severe CM among all CM cases (database of NCDF)

[f] Minimum additional cost of treatment for severe CM cases was considered 3 doses of *trimethoprim/sulfamethoxazole* as systemic antimicrobial and 1 dose of flunixin meglumine as anti-inflammatory drug for a cow with average body weight

[g] Mean cost of 1 litre reconstituted milk replacers for calves based on mixing directions and cost of used brands

[h] Average ratio of second to first parity lactational curve coefficients (Friggens et al., 1999)

[i] Hourly wage (Statistics Canada, 2015)

[j] required time in hours for disinfection of all teats of 1 cow

[k] assumed number of herd milking times/24 hours

[l] number of days per year

[m] proportion of cows which were dried off in a herd per year

[n] required time in hours to administer dry cow therapy for 1 cow (van Soest et al., 2016a)

Chapter 3 – Discussion

3.1 Limitations and potential biases

Estimating cost of mastitis is difficult. Several biases can be introduced in the calculation. Those are dealt by using different approaches in different studies. In some studies, some of these biases are included in the model, whereas in others, assumptions are made to control their effect. In following paragraphs, five potential biases are explained.

First, being a multifactorial disease, mastitis could be associated with numerous risk factors attributed to cow, mastitis pathogen or cow's environment (see Table I). The multifactorial nature of mastitis, makes the economic impacts of this disease difficult to study as those factors could influence both mastitis occurrence and the subsequent cost. For example, in the study by Rollin et al. (2015), type of pathogen causing mastitis was included in the model, whereas in the study by Heikkila et al. (2012), this factor was not included in the model.

Second, some mastitis economic consequences are hardly measurable. For example, the pain inflicted by mastitis brings concerns about animal welfare with potential impacts on consumers' attitude toward consumption of dairy products (Hudson, 2010). The effects of pathogen spreading from untreated IMI and the increased risk of new IMI in herd mates is also difficult to quantify (Sommerhäuser et al., 2003). Moreover, when highly valuable cows are culled due to mastitis, effects of genetic value loss is hardly quantifiable (Heikkilä et al., 2012).

Third, many biosecurity practices are adopted in dairy farms to prevent several diseases in cows. Mastitis is one of the diseases that its risk of transmission is reduced when theses practices are implemented in the farm. However,it is difficult to determine whether the costs of these practices should be considered when estimating costs of mastitis. Indeed, these practices would probably still be used on farm if it was not for mastitis. For example, cleaning lanes and cubicles were included in cost estimation by van Soest et al. (2016a), while these preventive measure were not included in Yalcin and Stott (2001). If cost of biosecurity practices are included, it is difficult to determine the portion of these costs that should be attributed to mastitis.

Fourth, different cost components may have impacts on one another. For example, CM treatment protocol may have impacts on milk yield reduction subsequent to CM. The study by Shim et al. (2004) showed that using antibiotic in CM treatment can reduce milk loss in the rest of lactation to one third compared to using supportive treatment without antibiotic.

Fifth, estimated costs of mastitis in a study cannot be easily generalized. For example, the value of economic loss is influenced by type of production system. Production loss in intensive production systems is higher than in extensive systems (Huijps et al., 2008b).

The aim of this thesis was to present a rough, but robust and comprehensive approximation of mastitis costs in the current situation on Canadian dairy herds, and to measure the distribution of estimated costs across components. Therefore, those mastitis consequences for which the causative structure with mastitis is not perfectly clear were excluded from our economic model. For instance, the potential negative impact of mastitis on subsequent fertility was not considered (see explanations below). Furthermore, some assumptions were made to make the estimation process achievable.

One of the components of mastitis cost suggested by Halasa et al. (2007c) was the effects of mastitis on other diseases. Mastitis is demonstrated to be associated with higher risks of metritis, displaced abomasum, ketosis, and cystic ovary (Gröhn et al., 1989, Schrick et al., 2001, Santos et al., 2003); however, the causality of associations between mastitis and these health problems is still not clear. For instance, we cannot exclude the possibility that an extraneous factor is concurrently increasing mastitis risk and risk of these other health events. For instance, the cow immune system efficiency, which may be influenced by factors such as her genetic and diet, may both influence risk of mastitis and of metritis, with the later having subsequent negative impacts on reproductive performances. In such case, associations between mastitis and these health events reported in the literature would be the result of these unmeasured and uncontrolled confounders. For this reason, this component was not included in our calculations. If these associations were causal (i.e. if mastitis is indeed the cause for these health events), then excluding these from our calculation would have biased our results toward an underestimation of mastitis cost.

Although some studies showed that treatment of SCM during lactation could be efficient, some producers will postpone SCM treatment to dry-off to avoid discarding milk during the lactation (Oliver et al., 2004, Swinkels et al., 2005). Therefore, in the current study, it was assumed that SCM is not treated during lactation (assumption #1). In practice, some producers do treat SCM-affected cows during the lactation. Therefore, again, excluding the cost of these treatments and subsequent milk discard may have led to an underestimation of mastitis costs. Since there is currently a milk supply management system in Canada, estimated cost of milk yield reduction is different from that in countries without quota system. Without a quota system, the cost of one liter of unproduced or discarded milk is simply the market value of that amount of milk (i.e. one liter of milk is not sold and the producer did not receive any money for that amount of milk). For instance, in January 2015, dairy producers in the province of Québec received 0.80 CAD/L of milk (Les Producteur de lait du Québec, 2015), so without a quota system, the costs for the unproduced and discarded milk, would simply be 0.80 CAD/L × the volume of milk (assuming the price paid to dairy producers would remain the same). However, In a quota system, we can assume that unproduced milk by a given cow because of CM or SCM will have to be produced by other cows (Halasa et al., 2007). Otherwise the dairy producer will eventually have to give up quota, so the milk is not completely lost, it will be produced otherwise and sold anyway, and the extra costs associated with production of this milk, rather than the market value of the unproduced milk, should be used to estimate the economic impact of any milk reduction. To maintain quota, in Canada, two practical options are available for the producer: 1) keeping additional cows; or 2) increasing production of currently available milking cows (e.g. by increasing amount of concentrates in the ration). It's been shown that, when there is supply management system, producers tend to keep cows for a prolonged period of time beyond the decided culling time to compensate for unproduced milk due to mastitis (Swinkels et al., 2005), so they do keep more cow units on the farm, rather than increasing daily individual production (our assumption #2). To compute value of the unproduced and discarded milk we, therefore, used cost for production of one liter of milk. Therefore, we could hypothesize that the estimates obtained in the current study are valid only for a market with milk supply management and that, in order to extrapolate these estimates to dairy production systems without milk supply management, this assumption should be adjusted. However, based on the Cost of production study (Canadian Dairy Commission, 2016a) conducted in 2015, the estimated cost for production of one liter of milk was 0.78 CAD/L of milk, which is fairly close to the market value of that milk.

The milk that is withheld from bulk tank can be a potential source of nutrition for young calves in dairy farms, and many producers use it to feed the calves when the milk odor, color, and consistency appear normal (Moore et al., 2009). Therefore, in this study high SCC milk withheld from bulk tank was assumed to be totally fed to calves (assumption #3). On one hand, this practice brings economic profits, but on the other hand, it may cause economic losses. Feeding waste milk to calves is demonstrated to have unfavorable effects on their health and growth rate due to contamination with bacteria, bacterial toxins, or antibiotic residues that could be resistant to pasteurization (Aust et al., 2013). Furthermore, this practice is not commonly applied by all producers. Assuming that this practice was applied by all producers, and excluding the cost of undesirable impacts of such practice in our calculations, may have led, again, to a certain underestimation of mastitis costs.

It has been demonstrated that high SCC in milk have effects on shelf life of fluid milk and quality of dairy products (Ma et al., 2000, Santos et al., 2003). We assumed, however, that economic impacts of dairy product quality would affect the dairy processing companies solely and not dairy producers (assumption #4). More realistically, a loss of quality may influence consumers' attitudes toward milk consumption, which may in turn affect the total volume of milk sold, and, ultimately, dairy producers' quota and milk price, so, again, ignoring these costs, possibly led to an underestimation of the costs.

The studies that investigated the risk of mortality in mastitis, included CM solely (Thomsen et al., 2004, Bar et al., 2008a, Cha et al., 2013, McConnel et al., 2015) as it is impossible for IMI without clinical features to be lethal to the cow; therefore, in this study it was assumed that there was no death caused by SCM (assumption #5). We can hardly argue against this assumption and, therefore, we are not expecting any biases in our costs estimates because of this assumption.

The common purpose of all economic analyses is supporting decision making (Huijps et al., 2009). Although economic analyses can never be entirely complete as additional influencing elements are being recognised by time, and there are always some elements that have to be ignored because of practical considerations. Therefore, the role of economic models are to identify optimal decisions with the available knowledge of the disease (Marsh, 1999). In our case, we intentionally chose assumptions leading to an underestimation of mastitis costs. The direction of the bias is, therefore, known, and the reported mastitis cost could possibly be interpreted as the minimal cost. Despite this, we believe that the magnitude of the bias is relatively small, since the components ignored and the assumptions made were not influencing the most important costs components.

3.2 Main results

Most studies estimating cost of mastitis usually focused on a limited part of the cost, either on one component (e.g., milk production loss), or one form of the disease (e.g., CM only). There was only one study in The Netherlands covering costs attributed to all components of CM, SCM, and preventive measure (van Soest et al., 2016a). Besides, there is noticeable variation in estimated costs in different studies conducted in different countries (Huijps et al., 2008b); therefore, instead of comparing absolute estimated costs solely, comparing the relative costs of different components bring another important level of information.

Estimated cost of clinical mastitis

In the current study, median cost of CM was estimated at 744 CAD/case, and the three most important components for CM cost were culling, milk yield reduction, and discarded milk. Several studies estimated cost of CM in different regions of the United States. The average cost of CM was estimated $179/case in New York state by Bar et al. (2008b). The estimated cost in this latter study varied based on milk price and cow production level before developing mastitis. The three most important CM cost components were milk yield reduction, treatment associated cost, and increased mortality. In another study, cost of CM was estimated at $ 211, $ 134, and $ 95/case for gram negative, gram positive, and other agents causing CM, respectively. The main components that constituted these estimated costs were different for each mentioned category. The main component for gram positive and other pathogen CM was treatment; whereas milk yield reduction was the first component for cost of gram negative CM (Cha et al., 2011). In the study by Rollin et al. (2015), cost of an average CM case occurring in first 30 days of lactation was estimated $ 444/case. The three most important components of the estimated cost were culling and replacement, milk yield reductions, and therapeutics, respectively. In the study by Rollin et al. (2015), in herds that used waste milk from CM cases to feed calves, the cost of discarded milk component was considered $ 0, but according to producer reports in the current study 25% of waste milk were fed to calves and the rest had inacceptable appearance and was discarded.

In European countries, there were also some studies estimating cost of CM per case. In The Netherlands, average cost of CM was estimated € 210/case (Huijps et al., 2008b). This estimation varied from € 164 to € 235 based on stage of lactation when CM occurred. The three most important cost components were culling, drugs, and milk yield reduction respectively. A more recent study in the same country estimated cost of CM € 301/case (van Soest et al., 2016a) with milk loss, discarded milk, and culling to be the first three components. The study by Heikkila et al. (2012) in Finland, estimated cost of CM € 623/case for premature culling and € 458/case for optimal culling. Important cost components in Heikkila et al. (2012) study were milk yield reduction, veterinary services and drugs, and premature culling in CM cases that were culled, while important components in CM cost of cases who were not culled due to CM were milk yield reduction, veterinary services and drugs, and then discarded milk. In the study by Nielsen et al. (2010) in Sweden, estimated cost of CM was € 278/case, but the share of each component was not specified in this latter study.

There is, therefore, a large variation of CM cost depending on study, country, and period of time. Nevertheless, our results regarding cost of CM are comparable, although in the higher end, to those presented in other studies.

Estimated cost of subclinical mastitis

Although economic impacts of SCM have a bigger share in total mastitis cost, there are fewer studies measuring cost of SCM compared to CM cost. Evaluation of SCM is more difficult as diagnosis of SCM requires regular monitoring and record keeping, and case definition of SCM is controversial (Rollin et al., 2015). In addition, important components of SCM cost are mainly indirect.

In the current study, cost of SCM was estimated at 348 CAD/cow-year. In van Soest et al. (2016a) study in The Netherlands, cost of SCM was calculated at € 37/cow-year with a range of € 26 to 48 in different scenarios of labor wage and milk price. In the study by Yalçin (2000) in Scotland, cost of SCM was estimated at £ 85/cow-year, and estimated cost in herds with high and low BMSCC were of £ 102 and £ 35/cow-year, respectively. In Yalçin (2000) and van Soest et al. (2016a) studies, the only component of SCM cost considered was milk yield reduction. In the study by Huijps et al. (2009) in The Netherlands, cost of high SCC in early lactation (5-14 days after calving) of heifers were investigated by a different approach considering three possible scenarios for increased SCC. These scenarios were to be treated by producer, to turn into CM, or to continue in SCM. Then average cost of these three scenarios was estimated at € 31/heifer (range; 0 to 220). In this latter study, important components of the estimated cost were culling and milk yield reduction.

Regarding costs associated with SCM, we reported costs that are relatively higher than those of the previous studies. Of course, the context (different countries and periods of time) may explain the differences observed. However, the fact that we did consider the cost of milk yield reduction, discarded milk, veterinary services, diagnosis, and, most importantly, culling possibly explain the relatively higher cost observed in our study.

Estimated cost of mastitis preventive measures

In the current study, cost of preventive measures was estimated at 104 CAD/cow-year. van Soest et al. (2016a) calculated cost of prevention at € 120/cow-year by measuring a comprehensive list of practices including cleaning lanes and cubicles, keeping cows standing after milking, prestripping, wearing gloves during milking, washing dirty udders, disinfecting teats, milking high SCC cows last, rinsing clusters after milking CM cases, and dry off treatment. In another study by Yalçin (2000), cost of preventive practices were calculated at £ 26/cow-year that accounted for 18% of total mastitis cost. In this latter study, however, a limited number of preventive measures were included in calculations including dry cow therapy, teat disinfection, milking machine maintenance, and extra labor required for these measures, but culling was also included in the category of preventive measures.

Among the studies estimating mastitis cost, many studies did not include the cost of preventive measures (Østeras, 2000, Bar et al., 2008b, Huijps et al., 2008b, Heikkilä et al., 2012), and in the studies that included prevention cost, different approaches were used to estimate the cost of this component. For example, In some studies, the cost of labor required to apply preventive measures were not included (e.g. the labor needed for teat disinfection) (Gill et al., 1990b). In addition, the management practices included in the model varies among studies. In some studies, all management practices associated with mastitis prevention were included in the model (Huijps et al., 2010, van Soest et al., 2016a). This approach may result in overestimation of mastitis prevention cost because of some biosecurity practices. For example, cleaning lanes is implemented to prevent some other cow diseases such as lameness. In the current study, we decided to record cost associated with both application (labor) and materials (e.g. disinfectant, vaccine) of preventive measures that were strictly used for mastitis, since other measures would still be used if it was not for mastitis.

Moreover, for producer. the cost of getting these measures implemented in the farm is an important impediment for the adoption of preventive measures (Huijps et al., 2010). Therefore, the estimated cost in the current study could be used in future studies to evaluate cost-efficiency of management measures with regard to the economic benefits of decreasing CM incidence and/or BMSCC. This could be a source of motivation for dairy producers in Canada to adopt efficient management measures to control mastitis.

3.3 Future research

The results of the current Master thesis could be used to design economic models tailored for dairy production in Canada. By using databases from DHI, estimation on milk yield reduction would be more precise. The model could then be used to estimate cost of mastitis at herd level within a time period to support producers' decision-making process. These models could also be used for cost-efficiency studies on mastitis preventive practices that are currently adopted by Canadian dairy herds. Herd level mastitis cost can be used by dairy advisors to motivate dairy producers to make modifications in their udder health program.

By combining our model with the economical model developed with DHI database, the cost of mastitis at provincial and/or national level could be computed. This research has already begun and results will be available soon. Then we will be able to evaluate how mastitis costs have evolved over time (e.g. from 2000-2016) using DHI databases from different years. Such a regular estimation of mastitis cost at provincial or national levels could be used to monitor mastitis cost over time and identify opportunities for investments for controlling this endemic disease more efficiently. Furthermore, the economical model could also be used to quantify the potential economic profit from a given reduction of the SCC or of the IRCM at provincial or national level. Knowing the value of such economic benefits could encourage provincial milk boards to establish more attractive premiums systems.

Another interesting subject could be identifying preventable costs among components of mastitis cost by evaluating the effects of different screening protocols, treatments, culling and prevention strategies on total mastitis cost. This model could also be used to evaluate the cost-effectiveness of new mastitis control strategies that may be suggested by future studies.

3.4 Conclusion

Cost of mastitis on Canadian dairy farms is important A median cost of 662 CAD/cow-year was found. Among the different components of our model, milk yield reduction was the most costly component (313 CAD/cow-year; 46%). Cost for culling and implementation of preventive measures were the second and third respectively. In addition, cost due to SCM, CM, and preventive measures were estimated at 48%, 34%, and 15%, respectively.

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Annexe 1: French Questionnaire

Questionnaire sur l’impact économique de la mammite

Généralités

1. Combien de vaches en lait possédez-vous? ____________________vaches
2. Quelle est la production quotidienne moyenne de lait dans votre ferme? _________kg/jour
3. Combien vous coûte l’élevage ou l’achat d’une vache primipare? ____________$

4. Utilisez-vous du lait reconstitué pour nourrir vos veaux ?
   - o Non, passez à la question 5 SVP
   - o Oui

   4.a. Quelle marque de lait reconstitué avez-vous utilisé au cours des 12 derniers mois?

   ____

   4.b. Quel est le coût par kg de ces substituts laitiers ? _____________$/Kg poudre

5. Durant les 12 derniers mois, combien avez-vous dépensé sur les items suivants pour prévenir la mammite?

   5.a. Solution pour désinfection pré-traite des trayons ____________$/an

   5.b. Solution pour désinfection post-traite des trayons ____________$/an

   5.c. Traitement au tarissement ____________$/an

   5.d. Entretien de l’équipement de traite (inspection régulière, remplacement des pièces) ____________$/an

   5.e. Les gants pour les trayeurs ____________$/an

   5.f. Les serviettes pour essuyer les trayons ____________$/an

   5.g. Les vaccins contre la mammite (incluant coûts des vaccins et l’administration) ____________$/an

6. Est-ce que votre troupeau participait au programme de l'amélioration du troupeau laitier au cours des 12 derniers mois ?
   - o Non, passez à la question 7 SVP
   - o Oui

6.a. Combien de contrôle laitier avez-vous fait dans les 12 derniers mois? _____contrôle/an

6.b. Si ce n'était du CCS, est-ce que vous utiliseriez tout de même le contrôle laitier?

- o Non
- o Oui

La mammite clinique

Dans les questions suivantes, la mammite clinique est définit par une vache avec un lait anormal (flocons, eau dans lait…) avec ou sans apparition enflure du pis, fièvre, perte d'appétit…

7. Combien de cas de mammite clinique avez-vous eu au cours des 12 derniers mois? _______________cas de mammite clinique

8. Sur votre ferme, quelle proportion de vaches atteintes de mammite clinique traitez-vous avec des médicaments? ___________%

9. Quels médicaments sont utilisés afin de traiter les cas typiques de mammite clinique sur votre ferme?

Antibiotiques	Anti-inflammatoire (s'il y a lieu)
❍ 17900 special formula forte ❍ Cefa-lak ❍ Pirsue ❍ Spectramast LC ❍ Autre: _______________	❍ Anafen ❍ Metacam ❍ Banamine, Flunixine, Cronyxin ❍ Dexamethazone ❍ Flucort ❍ Predef 2X ❍ Autre: _____________

10. Combien de fois par jour et pour combien de jour l'antibiotique est-il administré? _________fois par jour, pendant __________jours.

11. Quel est le coût du traitement typique d'un cas de mammite clinique?
____________$/traitement (traitement complet)

12. Combien de temps le personnel de ferme passe-t-il à s'occuper d'un cas typique de mammite clinique (traitement initial et suivi, traite individuelle, etc...)?
_____________heures

13. Pour les cas de mammite clinique non traités, pendant combien de jours en moyenne jetez-vous le lait? ___________jours

    - Non applicable

14. Quelle proportion de lait des vaches ayant une mammite clinique utilisez-vous pour nourrir les veaux? ___________%

15. Pour quelle proportion des cas de mammite clinique appelez-vous un vétérinaire?
____________%

16. En moyenne, quel est le coût d'une consultation vétérinaire lors d'un cas de mammite clinique (indépendamment du coût des médicaments)? _____________$

17. Combien d'échantillons de lait ont été collectés et analysés (au laboratoire ou directement à la ferme) suite à des cas de mammite clinique au cours des 12 derniers mois? ______________échantillons/an

18. Quel est le coût d'un test réalisé en laboratoire? ___________$/test

19. Combien de vaches primipares ou multipares ont été réformées ou sont mortes suite à un cas de mammite clinique au cours des 12 derniers mois?
    _______vaches primipares réformées
    _______vaches primipares mortes
    _______vaches multipares réformées
    _______vaches multipares mortes

20. Lorsque vous réformez une vache avec mammite clinique, combien recevez-vous pour la vente de l'animal (viande ou lait)? _______________$

21. Combien dépensez-vous pour éliminer la carcasse d'une vache morte suite à une mammite clinique? _____________$

22. Avez-vous une couverture d'assurance pour les résidus d'antibiotiques dans le réservoir de lait?
    - o Oui
    - o Non

23. Si oui, quel est le coût de cette assurance? _________________$/an

Comptage de cellules somatiques (CCS)

24. Quel était le comptage des cellules somatiques moyen dans le réservoir de lait dans les 12 derniers mois? _____________*1000 cellules/ml

25. Combien avez-vous perdu en pénalités pour avoir dépassé la limite de CCS au cours des 12 derniers mois? ________$

26. Combien d'échantillon ont été collectés et analysés (au laboratoire ou directement à la ferme) pour des vaches à CCS élevé au cours des 12 derniers mois? ______________échantillons/ an.

27. Combien de vaches avez-vous exclue du réservoir de lait en raison d'un CCS élevé au cours des 12 derniers mois? _______________vaches

28. Durant combien de jours en moyenne excluez-vous le lait de ces vaches? ___________jours

29. Y-a-t' il une prime pour la qualité du lait dans votre province?
    - o Oui
    - o Non

30. Combien avez-vous dépensé au cours de 12 derniers mois pour un avis professionnel concernant la santé du pis autre que le traitement d'un cas de mammite clinique (ex : surveillance de routine, investigation d'épidémie, problème de CCS élevé) ? _________$/an

31. Combien de vaches primipares ou multipares ont été réformées suite à un CCS élevé au cours des 12 derniers mois?

________vaches primipares

________vaches multipares

32. Lorsque vous réformez une vache avec CCS élevé, combien recevez-vous pour la vente de l'animal (viande ou lait)? _______________$

Nous vous remercions pour le temps que vous nous avez accordé en répondant à ce questionnaire.

Annex 2: English Questionnaire

Economic of mastitis questionnaire

General

1. How many milking cows do you currently have? __________________cows
2. What is the cow average daily milk production on your farm? ___________kg/day
3. How much does it cost to rear or buy a first lactation cow? __________________$
4. Do you use milk replacer to feed the calves?

- ❍ No – if No, please proceed to question 5
- ❍ Yes
    - 4.a. What brand of milk placer did you use during last 12 months? ____________
    - 4.b. What are the costs per kilogram of milk replacer? _________$/Kg powder

5. During the last 12 months, how much did you spend on these items to prevent mastitis?

    - 5.a. Pre milking teat-disinfection solution _________________$/year
    - 5.b. Post milking teat-disinfection solution _________________$/year
    - 5.c. Dry cow therapy _________________$/year
    - 5.d. Milking machine maintenance (regular inspection by technician, replacing parts and liners) _________________$/year
    - 5.e. Gloves for milking personnel _________________$/year
    - 5.f. Towels for drying teats during milking _________________$/year
    - 5.g. Vaccine against mastitis (costs for vaccine and administration) _________________$/year

6. was your farm participating in Dairy Herd Improvement (DHI) control in last 12 months?

- ❍ No – if No, pleases proceed to question 7
- ❍ Yes
    - 6.a. How many controls in the last 12 months? __________controls/ year
    - 6.b. If it was not from SCC measurements, would you still use DHI control?
        - o No
        - o Yes

Clinical mastitis

In the current questionnaire clinical mastitis is defined as: a cow with abnormal milk (flakes, watery…) with or without a swollen udder, fever, loss of appetite…

7. How many cases of clinical mastitis did you have in the last 12 months? _________CM cases

8. On your farm, what proportion of cows with clinical mastitis is treated with drugs? _________%

9. What drugs are used to treat a typical clinical mastitis case on your farm?

Antibiotics	Anti-inflammatory (if any)
❍ 17900 special formula forte ❍ Cefa-lak ❍ Pirsue ❍ Spectramast LC ❍ Other: _______________	❍ Anafen ❍ Metacam ❍ Banamine, Flunixine, Cronyxin ❍ Dexamethazone ❍ Flucort ❍ Predef 2X ❍ Other: _____________

10. How many times per day and for how long is the antibiotic administered?
__________________times per day, for __________________days

11. What is the cost of your typical clinical mastitis treatment? __________________$/ treatment (complete whole treatment)

12. How much time do the farm personnel spend working on a typical clinical mastitis case (initial and follow-up treatments, separate milking, etc)? _______________hours

13. For clinical mastitis cases that are not treated, on average for how many days do you discard the milk? __________________days

❍ Not Applicable

14. What proportion of discarded milk from cows with clinical mastitis is used to feed the calves? __________________%

15. In what proportion of clinical mastitis cases do you call a veterinarian? __________________%

16. On average what are the costs of the veterinarian when called for a clinical mastitis case (without cost of drugs)? __________________$

17. How many milk samples were collected and analyzed (sent to the lab or analyzed on-farm) for clinical mastitis cases in the last 12 months? __________________samples/year

18. How much do the laboratory tests cost? __________________$/test

19. How many 1st lactation and older cows were culled or died due to clinical mastitis in the last 12 months?

______1st lactation cows culled

______1st lactation cows died

______older cows culled

______older cows died

20. When culling a cow with clinical mastitis on average how much money is received for meat or milk sale? _________________$

21. How much money is spent on carcass disposal in case a cow dies from CM? _________________$

22. Do you have insurance coverage for antimicrobial residue in the bulk tank?
- ❍ Yes
- ❍ No

23. If yes, what is the cost of this insurance? _________________$/year

Somatic cell count

24. What was your average bulk milk somatic cell count in the last 12 months? _________________x 1,000 cells/ml

25. How much did you lose as penalty for exceeding the SCC limit in the last 12 months? _________________$

26. How many milk samples were collected and analyzed (sent to the lab or analyzed on-farm) for high SCC cows in the last 12 months? _________________samples/year

27. How many cows were excluded from bulk tank because of high SCC in last 12 months? _________________cows

28. For how many days on average did you exclude milk from these cows? _________________days

29. Is there a premium in your province for milk quality?
- ❍ Yes
- ❍ No

30. How much did you spend in the last 12 months for professional advices concerning udder health issues different than treatment of a clinical mastitis case (e.g. routine monitoring, outbreak investigation, high SCC problems)?
___________$/year

31. How many 1st lactation and older cows were culled due to high SCC last year?
______1st lactation
______older cows

32. How much money was received for meat or milk sale for cows culled because of high SCC? _________________$/cow

Thank you for your time, in completing this questionnaire